"A STUDY ON ASSESSMENT OF RENAL FUNCTIONAL RESERVE BY PROTEIN TOLERANCE TEST IN TYPE 2 DIABETES MELLITUS"

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON ASSESSMENT OF RENAL FUNCTIONAL RESERVE BY PROTEIN TOLERANCE TEST IN TYPE 2 DIABETES MELLITUS"** is a bonafide work done by **Dr. RAMESH.D,** Post Graduate student in the Department of General Medicine, Kilpauk Medical College, Chennai-10,under our guidance and supervision in partial fulfilment of the rules and regulations of **The Tamilnadu Dr. M.G.R. Medical University** for the award of **M.D. Degree Branch I (General Medicine)** during the Academic period from **2013 to 2016.**

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ACKNOWLEDGEMENT FROM THE GUIDE

This dissertation work done by **Dr. RAMESH.D,** titled **"A STUDY ON ASSESSMENT OF RENAL FUNCTIONAL RESERVE BY PROTEIN TOLERANCE TEST IN TYPE 2 DIABETES MELLITUS**" was under my supervision for the entire duration of the study and I ensure that the candidate followed the rules of the ethical committee.

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DECLARATION

I, solemnly declare that the dissertation entitled **"A STUDY ON ASSESSMENT OF RENAL FUNCTIONAL RESERVE BY PROTEIN TOLERANCE TEST IN TYPE 2 DIABETES MELLITUS"** is done by me at Kilpauk Medical College, Chennai – 10 during the academic year of 2013 to 2016 under the guidance and supervision of **Prof. Dr. S. MAYILVAHANAN, M.D.,** to be submitted to **The Tamilnadu Dr. M.G.R. Medical University** towards the partial fulfilment of requirements for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH – I.**

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Date:

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ABBREVIATIONS

ADA- American Diabetes Association

AGEs -Advanced Glycosylation End Products

AT- Angiotensin

BMI – Body Mass Index

BUN –Blood Urea Nitrogen

CAD- Coronary Artery Disease

CKD-Chronic Kidney Disease

CrCl- Creatinine Clearance

DM- Diabetes Mellitus

ESRD-End-Stage Renal Disease

e-GFR-Estimated Glomerular Filtration Rate

FPG- Fasting Plasma Glucose

GTT- Glucose Tolerance Test

HbA1C- Haemoglobin A1 C

MDRD-Modification of Diet in Renal Disease

PCR-Protein Creatinine Ratio

PPG-Post Prandial Blood Glucose

PTT-Protein Tolerance Test

TGF-β Transforming growth factor β

VEGF -vascular endothelial growth factor

CONTENTS

INTRODUCTION

INTRODUCTION

Diabetes Mellitus is in the potential epidemic state in India and referred to as the diabetic capital of the world. Diabetes mellitus is more prevalent in our nation and its incidence rate is increasing in alarming proportions. Over the past 2 decades, prevalence of diabetes mellitus in the world wide has increasing dramatically, from an estimated 30 million cases in 1985 to 177 million cases in 2000. As on current data, by the year 2030 more than 360 million people in worldwide will have diabetes mellitus. Although the prevalence of both the types of diabetes mellitus is increasing worldwide, the prevalence of type 2 diabetes mellitus is much more rapidly rising than other types due to more of obesity and sedentary lifestyle as countries become more industrialized. Worldwide estimates project that more number of individuals with diabetes mellitus will be in the age group of 45–64 years in 2030.

As per to the Diabetes Atlas published by the International Diabetes Federation (IDF), In India, there are an estimated 40 million people with diabetes mellitus in 2007 ,has risen to 60 million in 2009 and it is predicted to rise about 120 million people in 2025 by which time every 5^{th} diabetic person in the world would be an Indian. Diabetes

mellitus is one of the major cause of morbidity and mortality, but numerous studies indicate that diabetes is likely under reported as a cause of death. A recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was responsible for almost 3 million deaths annually (1.7–5.2% of deaths worldwide).

Diabetes mellitus is the most common cause of kidney failure[2], accounting for around 44 percent of new cases. It is a detrimental condition in which the renal system fails to clear the body of wastes. Kidney failure is the last stage of chronic kidney disease (CKD). Even though when diabetes mellitus is controlled, it can progress to CKD and kidney failure. Many number of people with diabetes mellitus do not develop CKD that is severe enough to progress to kidney failure. There are many number of factors[3] that interplay leading to kidney disease in diabetes mellitus which include genetic, diet, and other medical diseases, such as Hypertension. It has been documented in several studies that higher the blood pressure and plasma glucose levels, more the risk and progress to kidney failure. So there is a need to diagnose subnormal kidney function[4] at an earlier stage in order to initiate treatment to prevent the progression of kidney damage.

Glucose tolerance test (GTT) has been used to diagnosis the diabetes mellitus in patients who are at risk. The stress of glucose load in GTT unravels the patient with marginal pancreatic dysfunction. It has been suggested that similar to GTT, a protein tolerance test (PTT) may helpful to diagnose the individuals with subnormal renal function before the disease manifestation. Raising creatinine level is often considered the first sign of a real dysfunction, but now, it may not be so. Microalbuminuria, another test to diagnose early renal dysfunction and it has been used as a marker of endothelial dysfunction at present. By the time the serum creatinine levels increase, a good amount of irreversible kidney damage is done .so, now this stresses the need for the tolerance test on the kidney in patients who have low glomerular filtration rate.

An acute oral protein load causes a transient hyper filtration that might reveal a loss of glomerular permeability properties .So, acute protein load test is of great utility in revealing a silent glomerular filtration disturbance.

The stress of PTT will enable us to determine individuals with impaired functional reserve. The present study utilizes this principle to identify those patients with diabetes who are at risk of developing renal failure.

AIMS

&

OBJECTIVES

AIM OF THE STUDY:

1. To evaluate the usefulness of "Protein tolerance Test" as a method of measuring renal functional reserve & diagnose early renal dysfunction in Type 2 diabetes.

2. To compare the above with normal subjects

REVIEW OF LITERATURE

REVIEW OF LITERATURE

DIABETES MELLITUS

"Diabetes mellitus refers to a group of metabolic disorders causing hyperglycemia due to reduced insulin secretion or action or both and increased production and /or decreased glucose utilization." The metabolic derangement associated with Diabetes mellitus causes various complications that impose a huge burden to the individual, health care system and the country.[5]

CLASSIFICATION

Diabetes Mellitus can be classified into the following 4 major categories:-

"1. Type 1 Diabetes Mellitus (due to Pancreatic Beta cell destruction leading to absolute insulin deficiency)

2. Type 2 diabetes Mellitus (due to predominantly resistance with relative insulin deficiency)

3. Gestational Diabetes Mellitus (diagnosed first time during pregnancy in a previously non diabetic individuals)

4. Other Specific types of diabetes (due to some other causes)"

Table.1 Etiologic Classification of Diabetes Mellitus:

"I. Type 1 Diabetes Mellitus

a) Immune-mediated b) Idiopathic

II. Type 2 Diabetes Mellitus

III. Gestational diabetes mellitus

IV. Other specific types of diabetes:

A. Genetic defects of beta cell development or function characterized by mutations in:

1. Hepatocyte nuclear transcription factor (HNF) 4α (MODY 1)
2. Glucokinase (MODY 2)
3. HNF-1α (MODY 3)
4. Insulin promoter factor-1 (IPF-1; MODY 4)
5. HNF-1β (MODY 5)
6. NeuroD1 (MODY 6)
7. Proinsulin or insulin
8. Mitochondrial DNA
9. Subunits of ATP-sensitive potassium channel
10. Other pancreatic islet regulators/proteins such as *KLF11, PAX4, BLK, GATA4, GATA6, SLC2A2* (GLUT2), *RFX6, GLIS3*

B. Genetic defects in insulin action:

1. Type A insulin resistance
2. Leprechaunism
3. Rabson-Mendenhall syndrome
4. Lipodystrophy syndromes

C. Diseases of the exocrine pancreas—pancreatitis, fibro calculous pancreatopathy, pancreatectomy, cystic fibrosis, hemochromatosis, neoplasia, mutations in carboxyl ester lipase

D. Endocrinopathies—acromegaly, pheochromocytoma, aldosteronoma ,glucagonoma ,Cushing's syndrome, hyperthyroidism, somatostatinoma,

E. Drug- or chemical-induced—glucocorticoids, β-adrenergic agonists, vacor (a rodenticide), pentamidine, nicotinic acid, diazoxide, thiazides, calcineurin and mTOR inhibitors, protease inhibitors ,epinephrine ,hydantoins, asparaginase, α-interferon, , antipsychotics (atypical and others).

F. Infections— coxsackievirus, congenital rubella, cytomegalovirus,

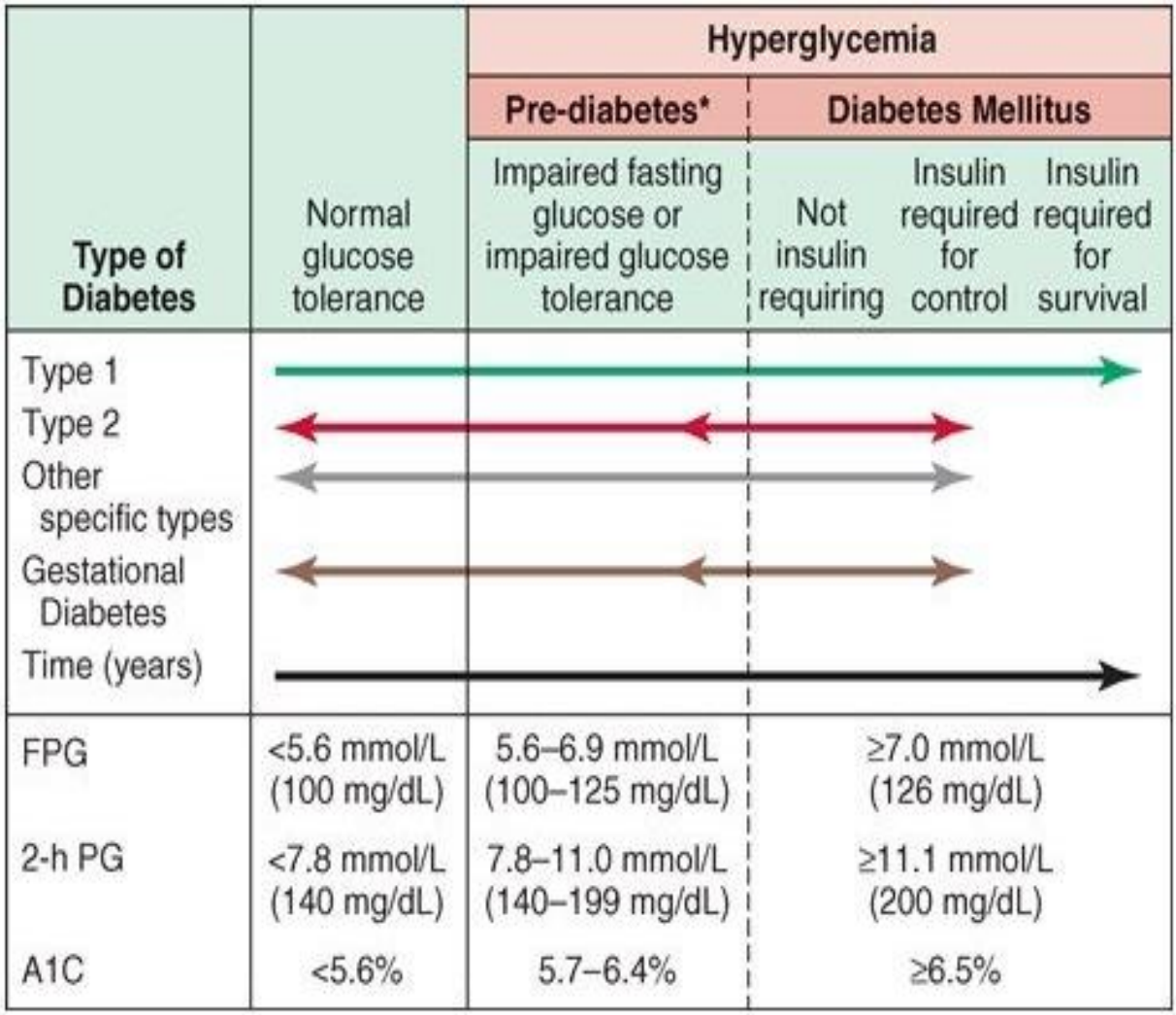
G. Uncommon forms of immune-mediated diabetes—stiff-person syndrome, anti-insulin receptor antibodies

H. Other genetic syndromes sometimes associated with diabetes—Klinefelter's syndrome, Down's syndrome, Wolfram's syndrome, Turner's syndrome, Friedreich's ataxia, Huntington's chorea, porphyria, Laurence-MoonBiedl syndrome, Prader-Willi syndrome ,myotonic dystrophy."

Abbreviation: **MODY, maturity-onset diabetes of the young**

Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as “impaired fasting glucose” (IFG) or “impaired glucose tolerance (IGT)” .These group of patients categorized as increased risk for diabetes or Pre diabetes or intermediate hyperglycemia.

Fig. 1 Spectrum of glucose homeostasis and Diabetes Mellitus[5]



-Values not applicable to the diagnosis of gestational DM.

DIAGNOSIS OF DIABETES MELLITUS

"Diagnosis of Diabetes is made by the following criteria[5] approved by American Diabetes association 2014.

Table 2. Diagnostic criteria of diabetes mellitus[5]

HbA1C	(or)	≥ 6.5%.
Fasting Plasma Glucose	(or)	≥126 mg/dL
2-h Plasma Glucose during an OGTT	(or)	≥200 mg/dL
Random plasma glucose (In a patient with classic symptoms of hyperglycemia or hyperglycaemic crisis)		≥200 mg/dL"

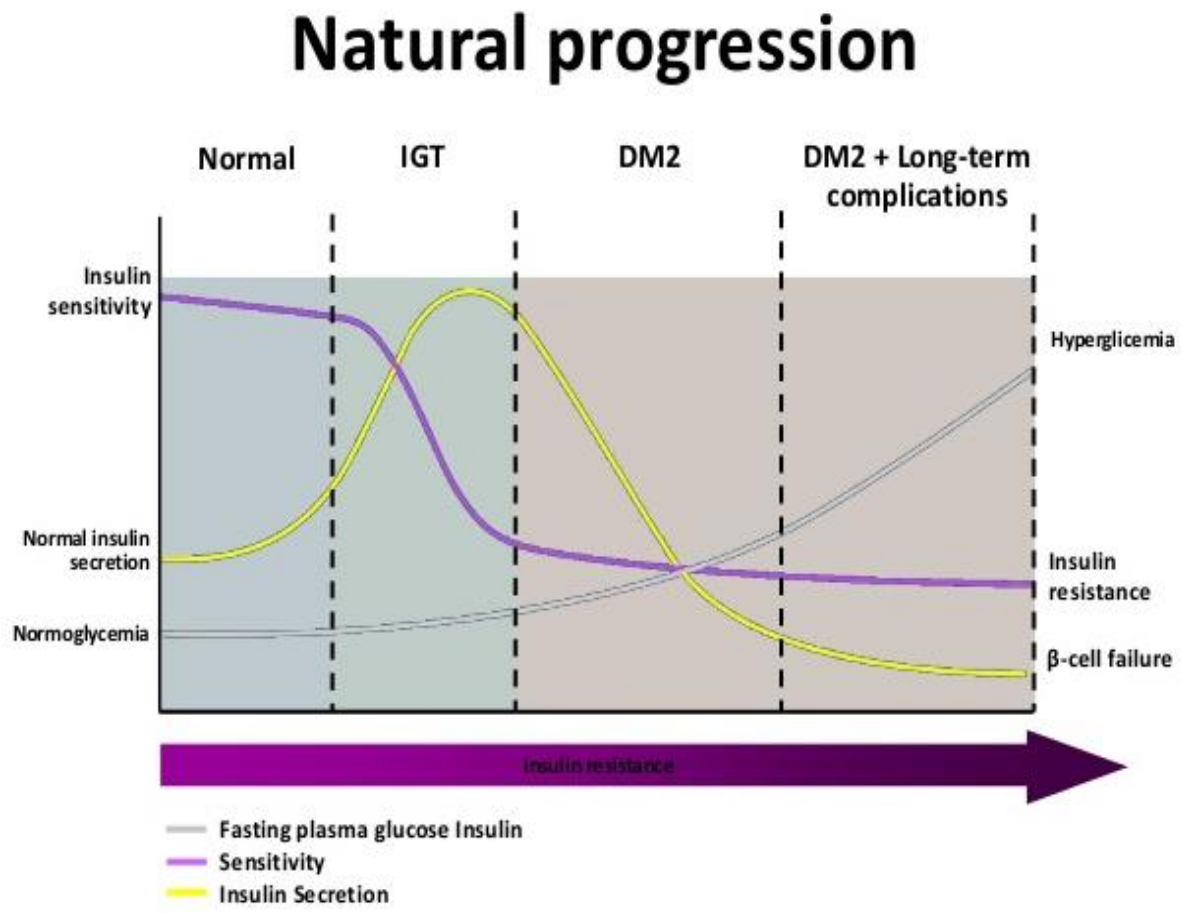
Prerequisites for Testing:

- "HbA1C test should be performed by the method that is NGSP certified and standardized to the DCCT assay.
- Fasting is defined as no caloric intake for at least 8 h.
- OGTT should be performed using a glucose load equivalent of 75g of anhydrous glucose dissolved in water , as described by the WHO,
- Random is defined as without regard to time since the last meal.
- In the absence of unequivocal hyperglycemia, diagnosis should be confirmed by repeat testing."

PATHOPHYSIOLOGY OF TYPE 2 DIABETES MELLITUS

Type 2 DM is characterized by "predominantly insulin resistance, impaired insulin secretion, hepatic gluconeogenesis, and abnormal lipid metabolism. Obesity, particularly visceral or central (as evidenced by the waist-hip ratio), is very common in type 2 DM (≥80% of patients are obese). In the early stages of the disorder, glucose tolerance remains near normal, despite insulin resistance, because the pancreatic beta cells compensate by increasing insulin output. As insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to sustain the hyperinsulinemic state. IGT, characterized by elevations in postprandial glucose, then develops. A further decline in insulin secretion and an increase in hepatic glucose production lead to overt diabetes with fasting hyperglycemia. Ultimately, beta cell failure ensues. Although both insulin resistance and impaired insulin secretion contribute to the pathogenesis of type 2 DM, the relative contribution of each varies from individual to individual."

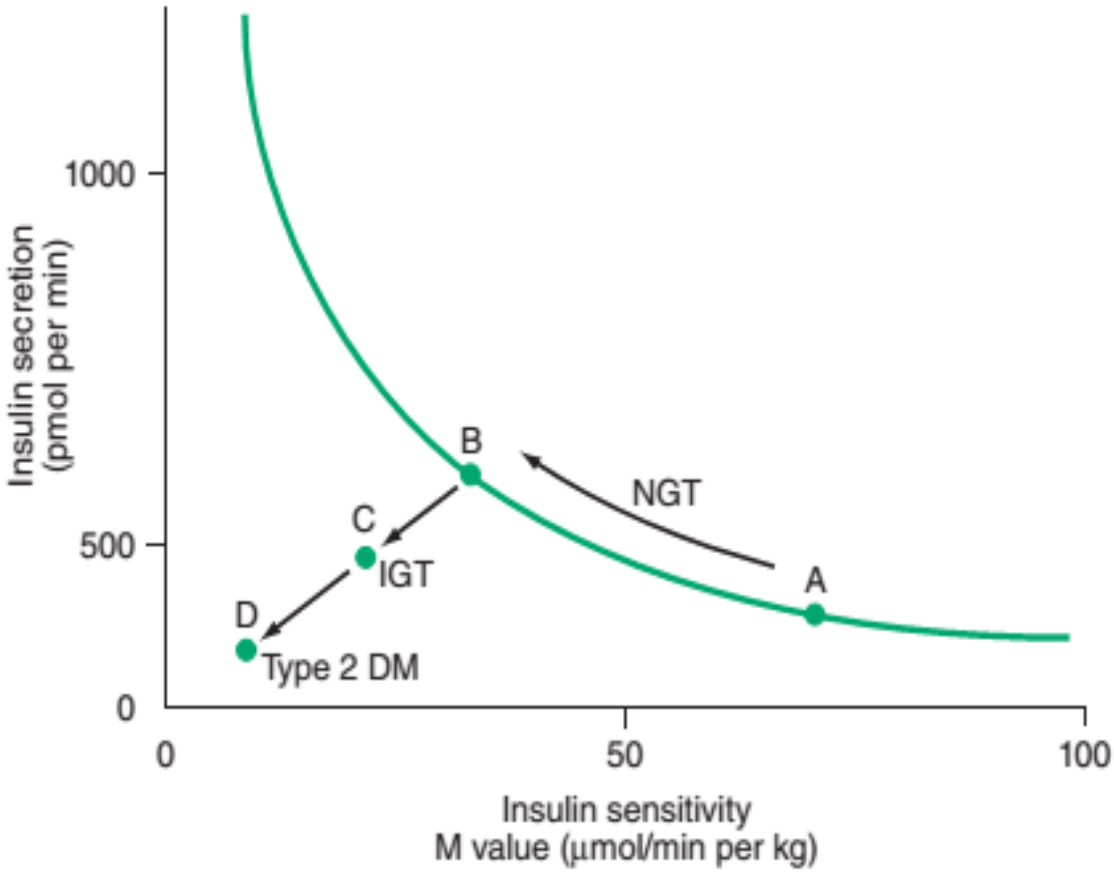
Fig.2. Natural Progression of diabetes Mellitus[5]



In Fig.3, "Insulin secretion and insulin sensitivity are related, and as an individual becomes more insulin resistant (by moving from point A to point B), insulin secretion increases. A failure to compensate by increasing the insulin secretion results initially in impaired glucose tolerance (IGT; point C) and ultimately in type 2 DM (point D)."

NGT-normal glucose tolerance.

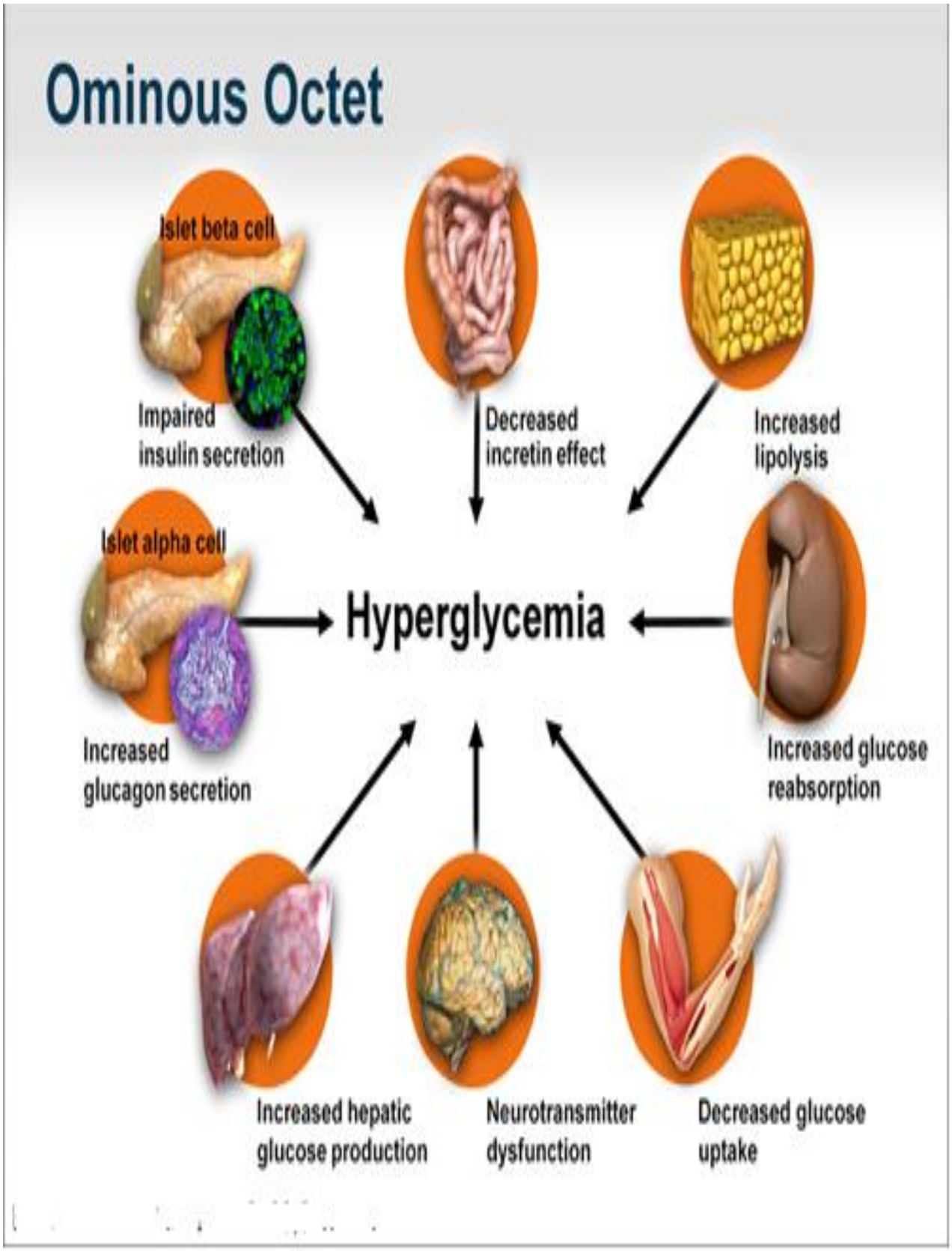
Fig. 3 Metabolic changes during the development of Type 2 DM



OMINOUS OCTET:

Finally and the most important, player to be implicated in the pathogenesis of type 2 diabetes mellitus is "the brain, which, along with his seven companions, forms the ominous octet".[45]

Fig. 4 Ominous Octet



COMPLICATIONS OF DIABETES MELLITUS:

Table 3 .Complications of Diabetes

<table>
<tr><td colspan="2">“ACUTE COMPLICATIONS:</td></tr>
<tr><td colspan="2">a) Hypoglycemia
b) Diabetic Keto Acidosis (DKA)
c) Hyperglycaemic Hyper osmolar state (HHS)</td></tr>
<tr><td colspan="2">CHRONIC COMPLICATIONS:</td></tr>
<tr><td>Microvascular:
• Nephropathy
• Retinopathy
• Neuropathy</td><td>Macrovascular:
• Coronary Artery Disease(CAD)
• Cerebro Vascular Disease (CVD)
• Peripheral Artery Disease (PAD)</td></tr>
<tr><td colspan="2">Others:
• GIT: (Gastroparesis, diarrhoea)
• Uropathy/sexual dysfunction)
• Dermatologic
• Infectious
• Cataracts, Glaucoma
• Cheiroarthropathy
• Periodontal disease
• Hearing loss”</td></tr>
</table>

DIABETIC NEPHROPATHY

The natural history of Diabetic Nephropathy in patients with type 2 DM is less well understood than in patients with type 1 DM. This partly reflects the fact that type 2 DM is largely a disease of an older population with associated obesity ,hypertension ,dyslipidemia and high rates of cardiovascular disease that restrict the manifestation of renal disease. In addition approximately 7% of the patients with type 2 DM already have microalbuminuria at the time of diagnosis. Within 5 years of diagnosis 18% have microalbuminuria especially those with poor metabolic control and high blood pressure levels[8.]

It is commoner to see more patients of type 2 DM with nephropathy than those with type 1 DM (9:1) even though the incidence of nephropathy is high in type 1 DM (30%) when compared to type 2 DM (20%) [9]

DEFINITION:

Nephropathy is one of the commonest complications of type 2 diabetes mellitus. "Diabetic nephropathy[10] (DN) is typically defined by macro albuminuria i.e. urinary albumin excretion of more than 300 mg in a 24-hour collection and abnormal renal function as represented by an abnormality in serum creatinine, calculated creatinine clearance, or

glomerular filtration rate (GFR)." Clinically, it is characterized by a progressive increase in proteinuria and progressive decline in GFR, hypertension, and a high risk of cardiovascular morbidity and mortality[11].

PREVALENCE:

Diabetes has become the major cause of end-stage renal disease (ESRD) and the incidence of type 2 diabetes mellitus is abruptly increasing worldwide. "Approximately 44% of new patients entering dialysis in the United States are diabetics[12] and 20% to 30% of all diabetics will develop evidence of nephropathy, although a higher percentage of type 1 patients progress to ESRD[13]."

RISK FACTORS:

"Risk factors for diabetic nephropathy[14] are shown in table 4.

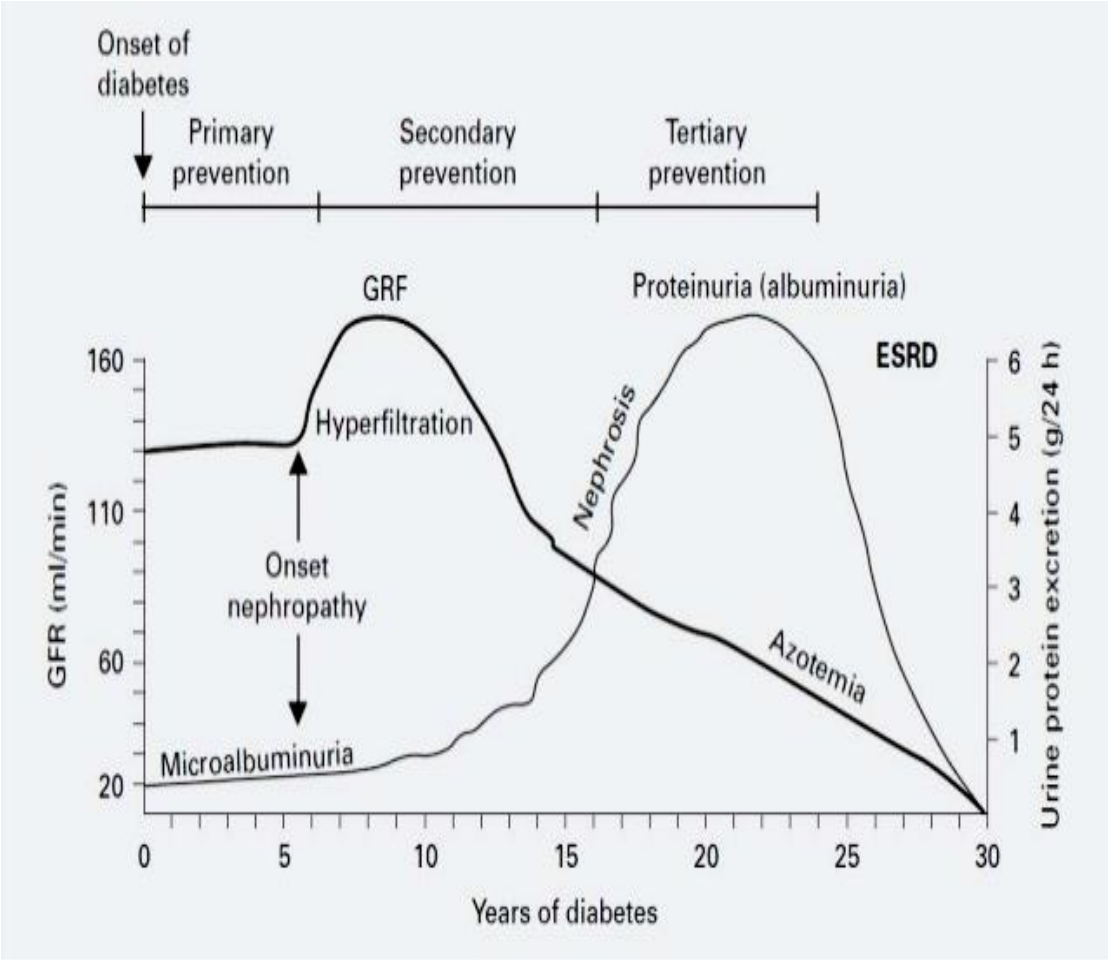
Table 4 .Risk factors for diabetic nephropathy

- African American, Hispanic, or American Indian origin
- Family history of kidney disease or high blood pressure
- Poor control of blood pressure
- -Poor control of blood glucose
- Type 1 diabetes before age 20
- Smoking"

PATHOPHYSIOLOGY AND NATURAL HISTORY:

The progression of nephropathy from "microalbuminuria to overt nephropathy has led many to consider microalbuminuria to define early or incipient nephropathy[15.]" Renal disease is suspected to be secondary to diabetes in the clinical setting of long-standing diabetes. This is supported by the history of diabetic retinopathy, particularly in type 1 diabetics, in whom there is a strong correlation.

Fig. 5. Natural history of Diabetic Nephropathy



"Early diabetes is heralded by glomerular hyper filtration and an increase in GFR. This is believed to be related to increased cell growth and expansion in the kidneys, possibly mediated by hyperglycemia itself. Microalbuminuria typically occurs after 5 years in type 1 diabetes.[16] Overt nephropathy, with urinary protein excretion higher than 300 mg/day, often develops after 10 to 15 years. ESRD develops in 50% of type 1 diabetics, with overt nephropathy within 10 years.

Fig. 6. Typical Progression of Diabetic Nephropathy [46]

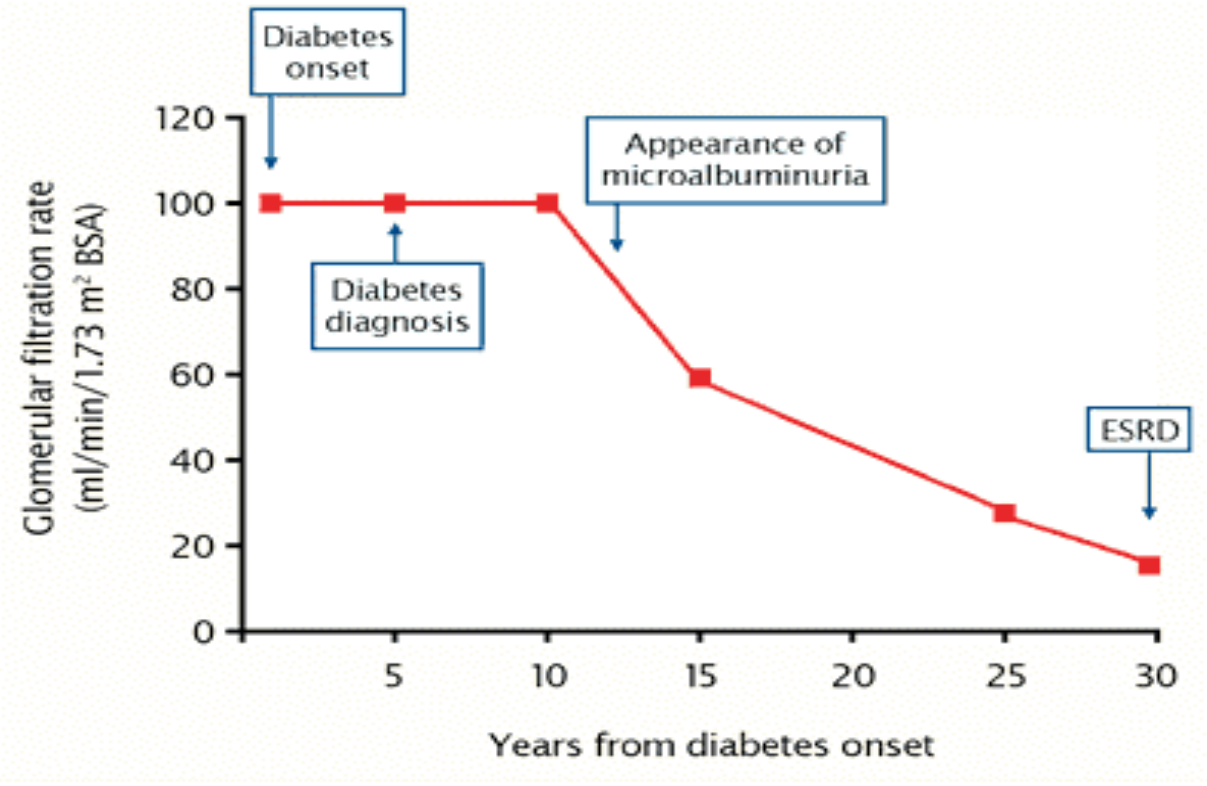
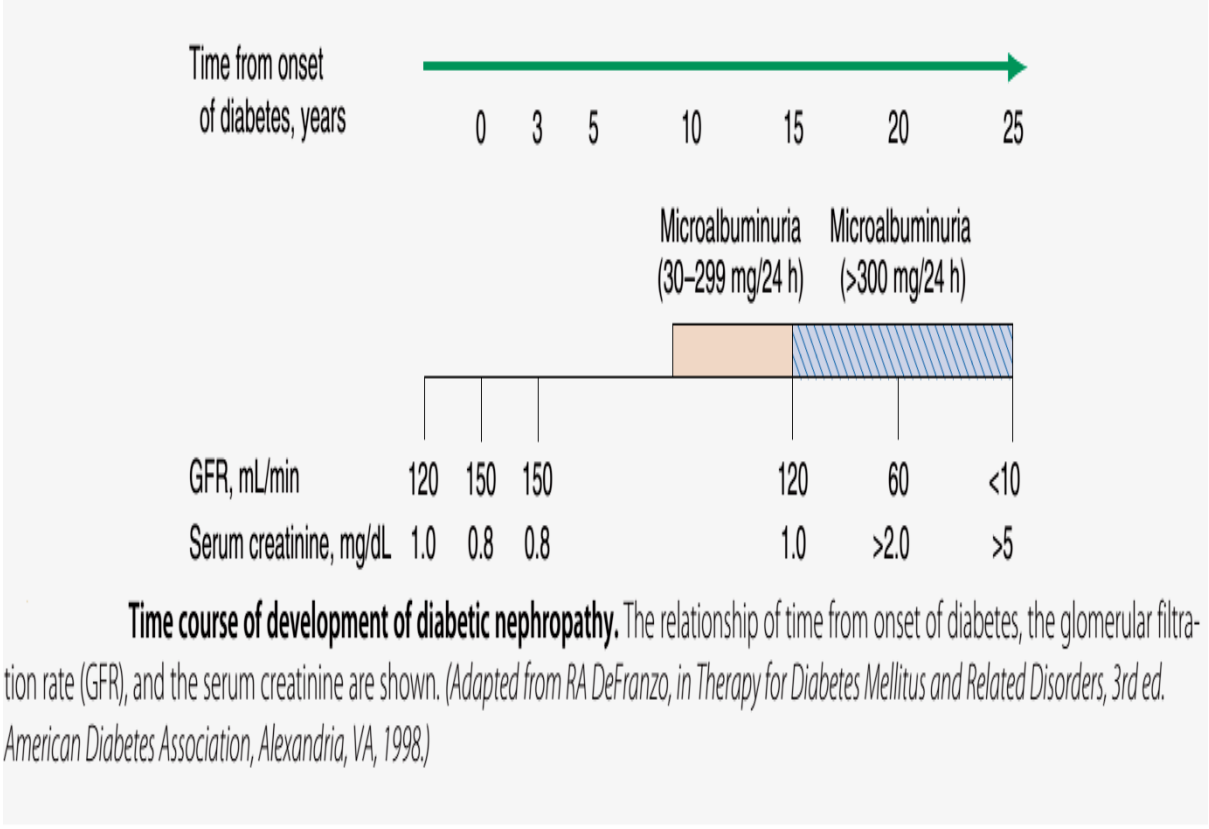


Fig. 7. Time course of development of Diabetic Nephropathy.

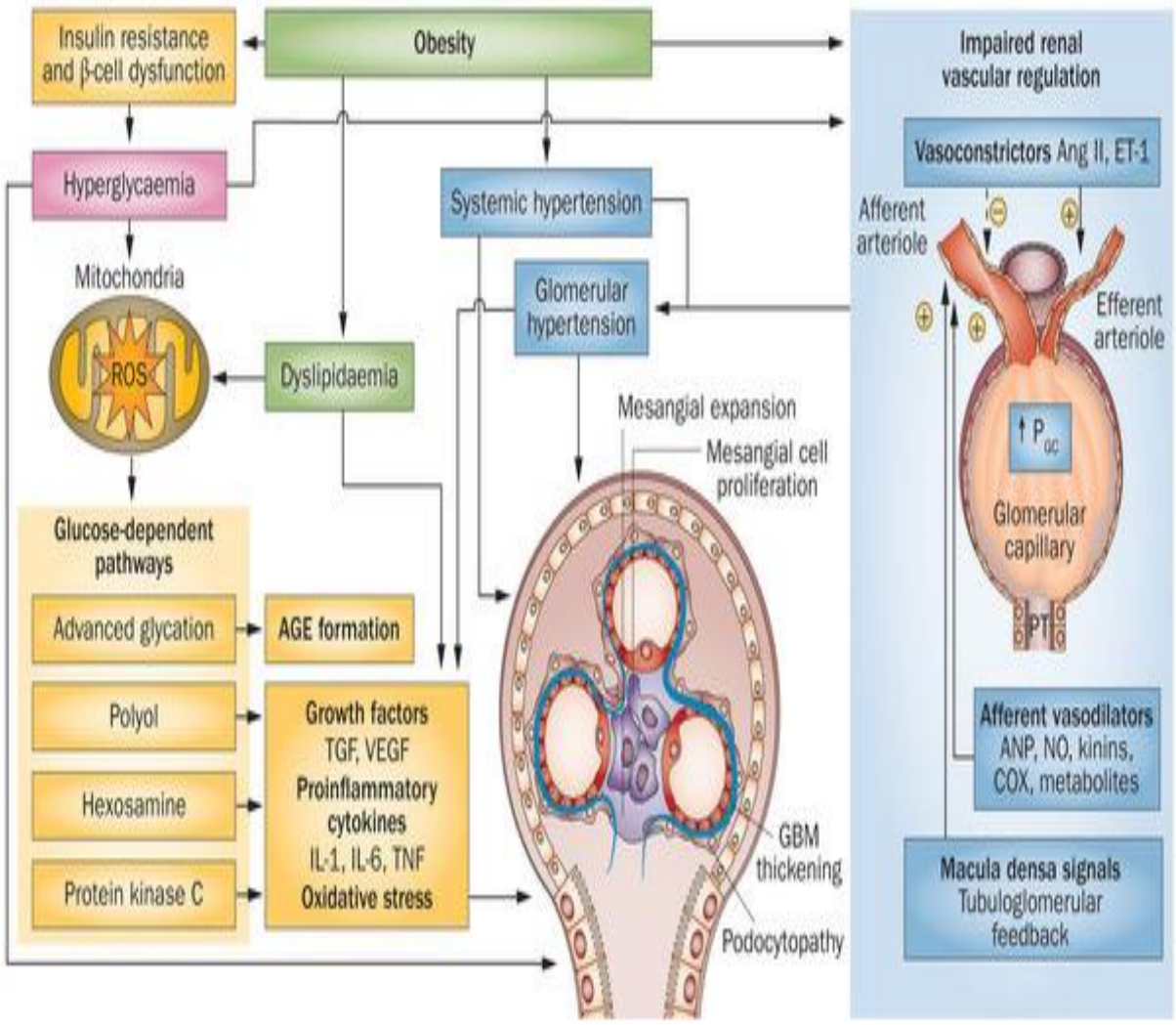


Time course of development of diabetic nephropathy. The relationship of time from onset of diabetes, the glomerular filtration rate (GFR), and the serum creatinine are shown. *(Adapted from RA DeFranzo, in Therapy for Diabetes Mellitus and Related Disorders, 3rd ed. American Diabetes Association, Alexandria, VA, 1998.)*

Type 2 diabetes has a more variable course. Patients often present at diagnosis with microalbuminuria because of delays in diagnosis and other factors affecting protein excretion. Fewer patients with microalbuminuria progress to advanced renal disease. Without intervention, approximately 30% progress to overt nephropathy and, after 20 years of nephropathy, approximately 20% develop ESRD. Because of the high prevalence of type 2 compared with type 1 diabetes; however, most diabetics on dialysis are type 2 diabetics.

Long-standing hyperglycemia is known to be a significant risk factor for the development of diabetic nephropathy.[17] Hyperglycemia may directly result in mesangial expansion and injury by an increase in the mesangial cell glucose concentration. The glomerular mesangium expands initially by cell proliferation and then by cell hypertrophy. Increased mesangial stretch and pressure can stimulate this expansion, as can high glucose levels.[18]

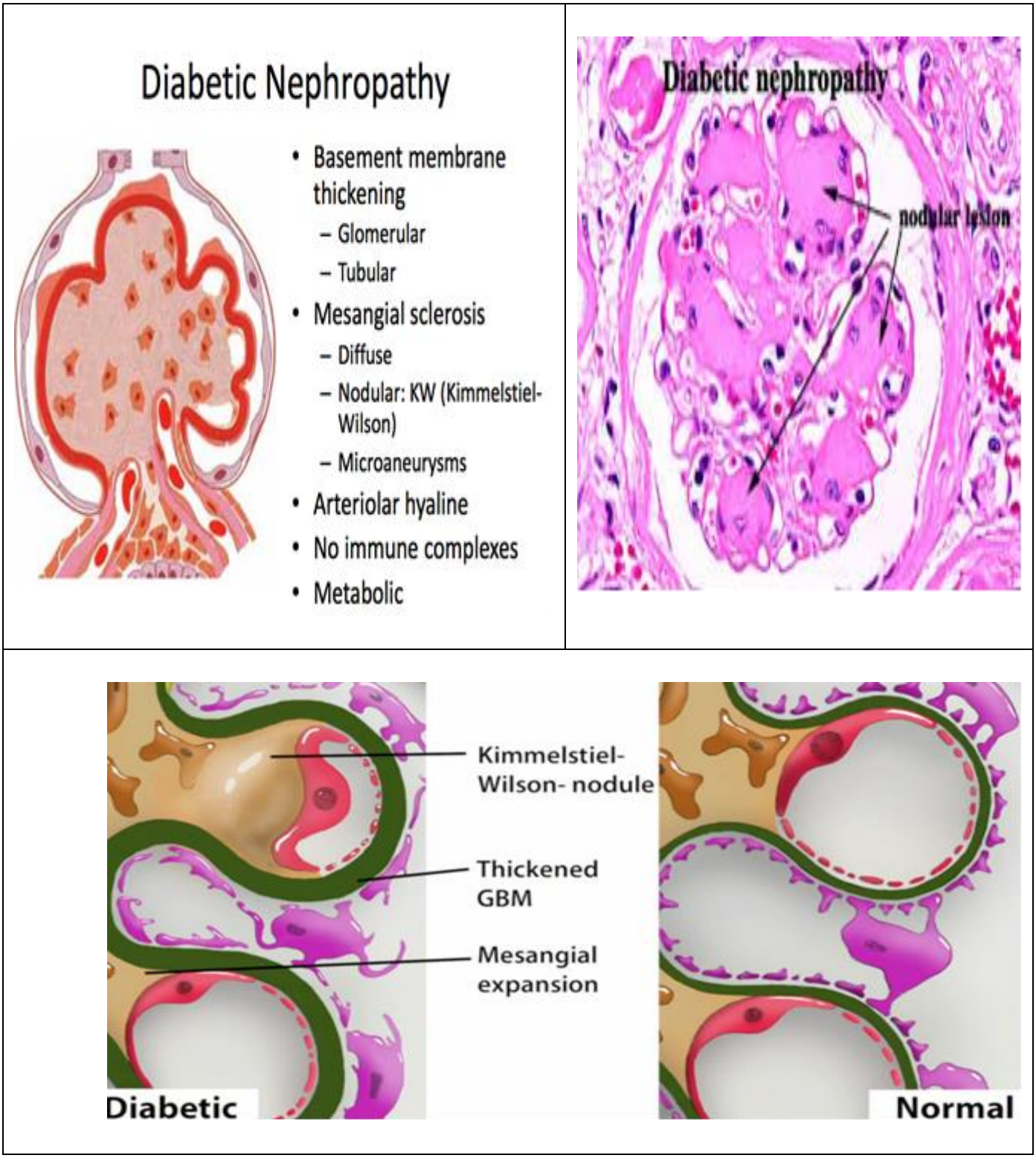
Fig. 8. Pathophysiological mechanisms of Diabetic Nephropathy:



Advanced glycosylation end products (AGEs) can form complex cross-links over years of hyperglycemia and can contribute to renal damage by stimulation of growth and fibrotic factors via receptors for AGEs. In addition, mediators of proliferation and expansion, including platelet-derived growth factor, TGF-β, and vascular endothelial growth factor (VEGF) that are elevated in diabetic nephropathy can contribute to further renal and microvascular complications.

In diabetic nephropathy, the activation of the local renin-angiotensin system occurs in the proximal tubular epithelial cells, mesangial cells, and podocytes. Angiotensin II (ATII) itself contributes to the progression of diabetic nephropathy. ATII is stimulated in diabetes despite the high-volume state typically seen with the disease, and the intrarenal level of ATII is typically high, even in the face of lower systemic concentrations. ATII preferentially constricts the efferent arteriole in the glomerulus, leading to higher glomerular capillary pressures. In addition to its hemodynamic effects, ATII also stimulates renal growth and fibrosis through ATII type 1 receptors, which secondarily upregulate TGF-β and other growth factors.”

Fig . 9.1-9.3 Pathological Features of Diabetic Nephropathy



THE COURSE OF KIDNEY DISEASE IN DIABETES

Diabetic kidney disease takes many years to develop. In some people, "the filtering function of the kidneys is actually higher than normal in the first few years of their diabetes. Over several years, people who are developing kidney disease will have small amounts of the blood protein -albumin begin to leak into their urine. This first stage of CKD is called microalbuminuria." The kidney's filtration function usually remains normal during this period. "As the disease progresses, more albumin leaks into the urine.[25] This stage may be called macro albuminuria or proteinuria."

Fig. 10 Stages of Diabetic Nephropathy according to Urinary Albumin level :

Stages of Diabetic Nephropathy According to Urinary Albumin Level			
Stage of nephropathy	**Urine dipstick for protein**	**Urine ACR (mg/mmol)**	**24 hour urine collection for albumin**
Normal	Negative	<2	<30 mg/day
Microalbuminuria	Negative	2-20	30-300 mg/day
Overt nephropathy	Positive	>20 >67	>300 mg/day >1000 mg/day
Values are for urinary albumin, not total urinary protein, which will be higher than urinary albumin levels. ACR results may be elevated with conditions other than diabetic nephropathy			

"As the amount of albumin in the urine increases, the kidneys' filtering function usually begins to drop. The body retains various wastes as filtration falls. As kidney damage develops, blood pressure often rises as well. Overall, kidney damage rarely occurs in the first 10 years of diabetes, and usually 15 to 25 years will pass before kidney failure occurs. For people who live with diabetes for more than 25 years without any signs of kidney failure, the risk of ever developing it decreases. People with diabetes should be screened regularly for kidney disease[26]."

DIAGNOSIS OF CKD

Fig.11 Diagnostic criteria of CKD:

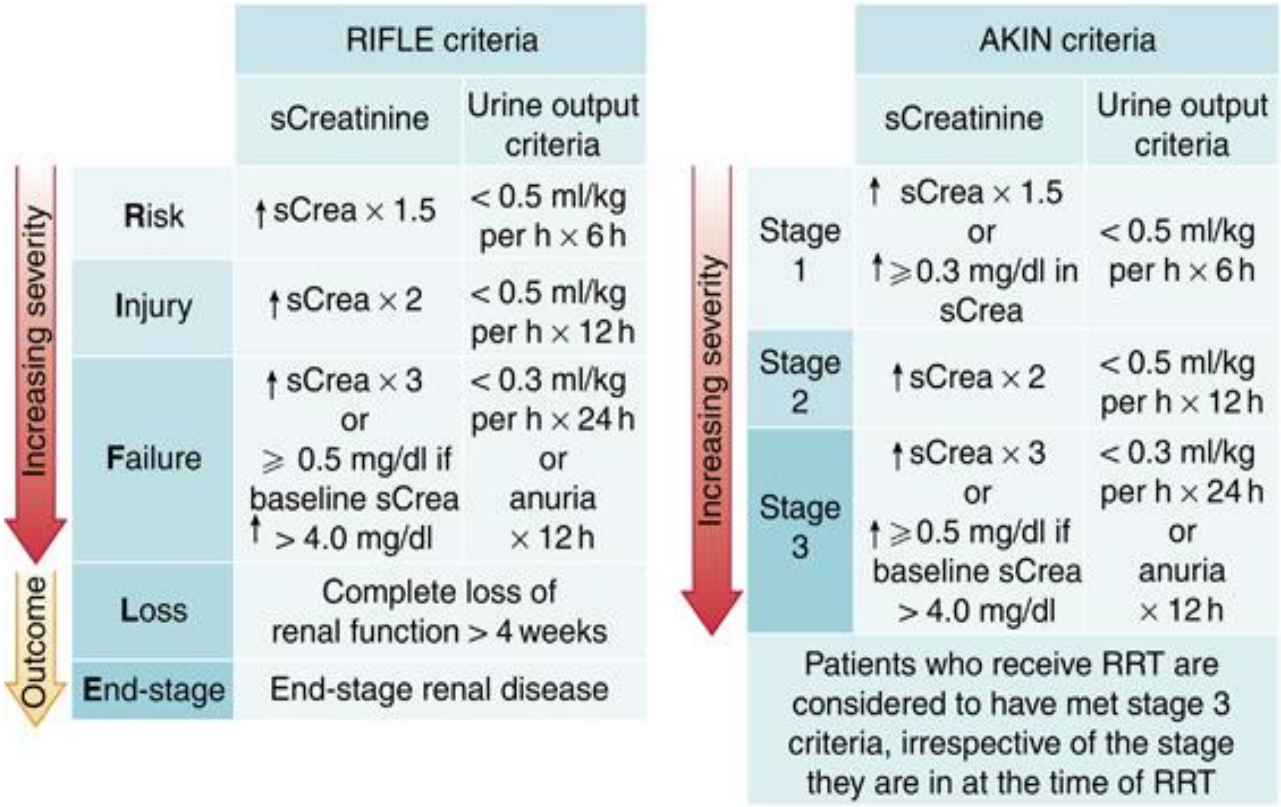


Fig.12 Stages of CKD:

Stages of Chronic Kidney Disease (K/DOQI)*

Stage	Description	GFR (ml/min/1.73m^2)
1	Kidney damage with normal or ↑GFR	≥ 90
2	Kidney damage with mild ↓GFR	60 - 89
3	Moderate ↓GFR	30 - 59
4	Severe ↓GFR	15 – 29
5	Kidney failure	< 15 (or dialysis)

The two key markers for kidney disease are eGFR and urine albumin eGFR stands for estimated glomerular filtration rate[27]. The calculation of eGFR is based on the amount of creatinine, a waste product, found in a blood sample. As the level of creatinine goes up, the eGFR goes down. "Glomerular filtration rate (GFR) measures the amount of glomerular filtrate (a substance similar to the plasma part of blood but without the proteins) formed in the kidneys per minute. The results help indicate the kidney's ability to filter and remove waste products from the body."

Types and differences of GFR

The glomerular filtration rate (GFR) of the kidneys cannot be directly measured. However, various methods have been developed to provide indirect measurements and estimates.[30]

Inulin Clearance Test:

"Inulin, a complex fructose sugar is considered an ideal filtration marker for the measurement of GFR in humans. Inulin is injected into the patient and the amount of inulin filtered at the glomeruli (blood vessels in the kidney) normally equals the amount of excreted inulin." However, this method is not often used because it is costly, inconvenient and better suited for research studies.

Radioactive marker clearance test:

The use of radioactive markers also provides an accurate measurement of GFR.[32] However, they are not readily available .

Serum creatinine and creatinine clearance:

It is the most commonly used method to measure the GFR. "Creatinine is a waste product that comes from two sources: meat products in the diet and muscle use. Almost all creatinine eventually ends up in a person's urine. Creatinine measurements from blood and urine samples are used to calculate GFR because the chemical is normally present in the body and very little of it is reabsorbed."

A creatinine clearance test compares the levels of creatinine in the urine and the blood, along with urine volume. A 24-hour urine sample is usually collected and a blood sample is taken from a vein, and the estimated GFR is calculated.

Serum creatinine based prediction equations

Serum creatinine based prediction equations are more accurate in estimating GFR than serum creatinine measurements alone. The equations are useful because they take into consideration that creatinine production varies according to age, gender, race or ethnicity, and muscle mass.

Fig.13. Equations to estimate GFR from Creatinine

Equations to Estimate GFR from Serum Creatinine Concentration

Adults	
Cockcroft-Gault equation [123]	$C_{Cr}(\text{ml/min}) = \frac{(140 - Age) \times Weight}{72 \times S_{Cr}} \times (0.85 \text{ if female})$
Abbreviated MDRD Study equation [124, 125]	$GFR(\text{ml/min/1.73m}^2) = 186 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African - American})$
Children	
Schwartz formula [126*]	$C_{Cr}(\text{ml/min}) = \frac{0.55 \times Length}{S_{Cr}}$
Counahan-Barratt equation [127]	$GFR(\text{ml/min/1.73m}^2) = \frac{0.43 \times Length}{S_{Cr}}$

GFR, glomerular filtration rate; C_{Cr}, creatinine clearance; S_{Cr}, serum creatinine in mg/dL; age, in years; weight, in kg; length, in cm.
*Formula for children >1 year. Coefficients vary for low birth-weight infants to 1 year (0.33), term infants up to 1 year (0.45), adolescent girls (0.55), and adolescent boys (0.70)

"The Cockcroft-Gault and Jelliffe were originally developed for estimating creatinine clearance. However, they have been widely tested as predictors of GFR in adults.

A newly developed equation, the MDRD Study equation, also provides an estimate of GFR in adults. The abbreviated version of the equation is based on serum creatinine concentration, age, gender and race and is standardized for body surface area.

There are some drawbacks to using prediction equations. One is that the equations are much less accurate at measuring a higher range of GFR, such as occurs in a healthy person or in the early stages of chronic kidney disease. As a result, other indications of early kidney disease, such as proteinuria (abnormally high levels of protein in the urine) are needed to detect early deterioration in kidney function. In newly diagnosed type 2 diabetic patients, particularly those with a GFR >/=90 ml/min per 1.73 m2, both CG and MDRD equations significantly underestimate eGFR. This highlights a limitation in the use of eGFR in the majority of diabetic subjects outside the setting of chronic kidney disease.

There are also some situations in which the GFR estimate provided by a creatinine clearance test is more desirable than that based on a prediction equation. This is because certain individual variations (e.g., diet and muscle mass) are not taken into consideration in prediction equations.

- Extremes of age
- Extremes of body size
- Disease of the skeletal muscles
- Vegetarian diet
- Use of creatine (dietary) supplements
- Rapid changes in kidney function
- Amputation
- Malnutrition
- Muscle wasting
- Pregnancy"

Cystatin C :

"Cystatin C is found in most cells, is filtered from the circulation by the glomeruli and forms a fluid filtrate.[37] The cystatin C left in the filtrate is then reabsorbed by the body and not returned to the blood. In Renal dysfunction the cystatin C levels in blood increases, and the test can reflect the reduction in the formation of fluid filtrate. The increased levels of cystatin C may be detected before there is a decrease in the GFR." In addition, gender, muscle mass and race or ethnicity does not influence the test.

In general, “an estimated GFR ≥ 90 millilitres per minute per 1.73 square meters (mL/min/1.73 m²) is normal. The 1.73 m² value represents the average adult body surface area in square meters. An estimated GFR less than 90 mL/min/1.73 m² is abnormal.”

In addition to aging and kidney disease, there are several other factors that may affect GFR.

Fig14. Factors affecting the GFR :

Changes in renal blood flow
Changes in glomerular capillary hydrostatic pressure
Changes in systemic blood pressure
Afferent or efferent arteriolar constriction
Changes in hydrostatic pressure in Bowman’s capsule
Ureteral obstruction
Edema of kidney inside tight renal capsule
Changes in concentration of plasma proteins: dehydration, hypoproteinemia, etc (minor factors)
Changes in K_f
Changes in glomerular capillary permeability
Changes in effective filtration surface area

Table 5. Disease conditions affecting GFR

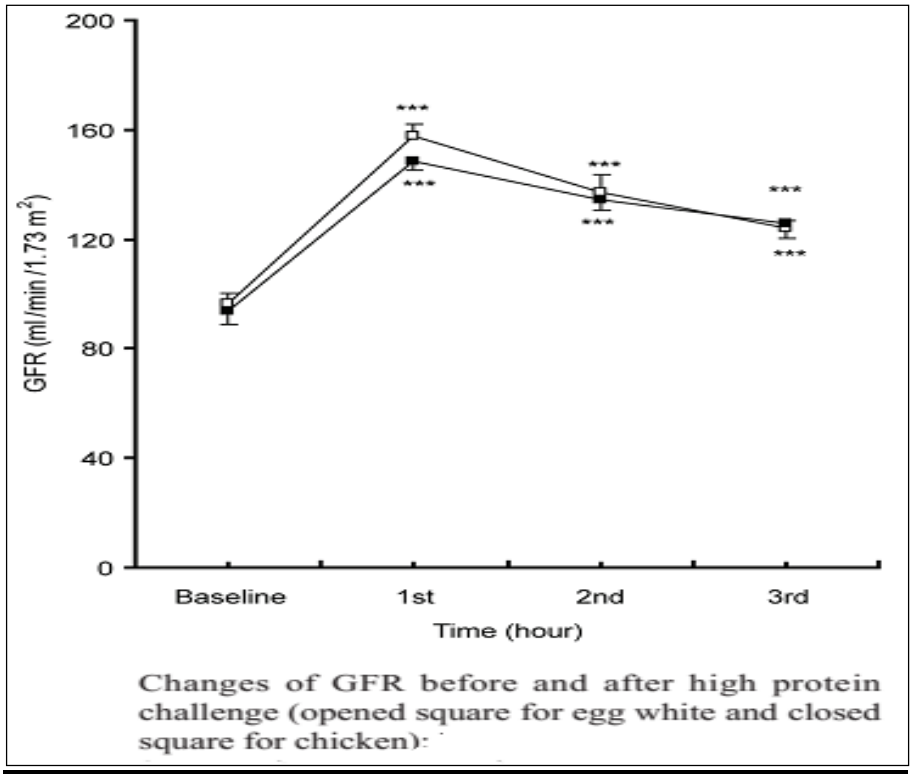
"Conditions that can decrease GFR:	**Conditions that can increase GFR:**
• Vascular disease • Congestive heart failure • Sodium and water depletion • Haemorrhage & shock • Vigorous exercise"	• Dietary protein intake • Ketoacidosis • Hyperglycemia • Pregnancy

PROTEIN TOLERANCE TEST[38]

"In this test, a patient is exposed to high level of protein and GFR is calculated in a span of two-three days, normally the GFR should increase by 20% without protein leaking into the urine.. The severity and prognosis of the renal disease is often predicted on basis of GFR."

A direct relationship was also found between the protein intake and GFR, i.e., "with an increase in protein intake there was an increase in GFR in both short term and long term studies. The possibility of a variation in GFR and the capacity of kidney to augment its level of function suggest a renal functional reserve[40]."

Fig 15. Changes in GFR after Protein meal



Changes of GFR before and after high protein challenge (opened square for egg white and closed square for chicken):

Renal Functional Reserve:

"The renal functional reserve represents the capacity of the kidney to increase its level of operation under certain demands. When the kidneys are subjected to greater physiological demands, they also respond with an increase in GFR."

In renal diseases, this functional reserve increases GFR of the residual nephrons, replacing the lost function and maintaining the whole organ GFR.[41] Only after the residual nephrons can no longer compensate for the functional loss, will the changes in resting GFR and rise in serum creatinine occur. On the other hand, the patient with a renal disease on a

low protein diet may have a reduction in GFR unrelated to the progression of renal disease. Resting GFR therefore is not only an insensitive index for early detection of renal disease but is also inappropriate for renal disease follow up.

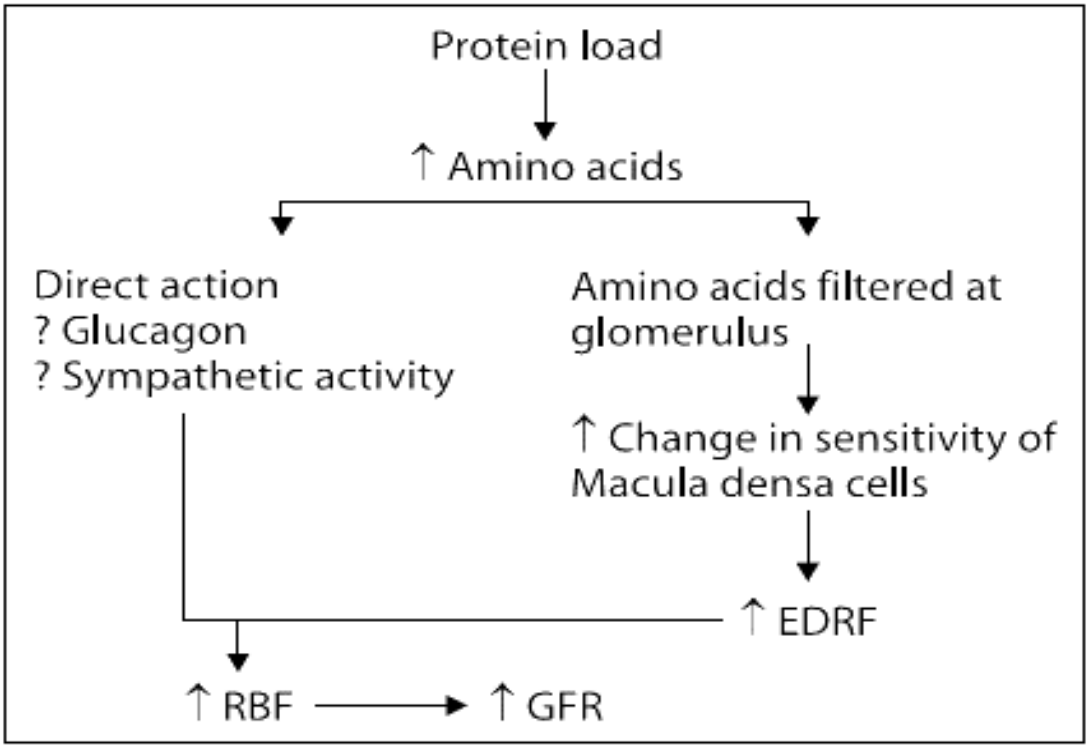
Glucose tolerance test (GTT) has been used to assess the patient at risk of diabetes mellitus. The stress of glucose load in GTT unravels the patient with marginal pancreatic dysfunction. It has been suggested that analogous to GTT, a Protein Tolerance Test (PTT) may help in identifying individuals with subnormal renal function before they manifest clinically. The stress of PTT will enable us to determine individuals with impaired functional reserve.[42] Thus PTT is a better test than resting GFR or serum creatinine

Mechanisms of renal hemodynamic response to protein feeding[43].

An acute oral protein load causes a transient hyper filtration that might reveal a loss of glomerular permeable selectivity properties. A protein meal, on digestion, "which acutely raises the plasma amino acid concentration similar to intravenous amino acid infusion. In a healthy metabolic state, the glomerulus filters these amino acids and acts directly on the kidney to stimulate proximal tubular absorption. Amino acid may also change sensitivity of the macula densa sensing mechanisms by

altering cell permeability. Sensing a reduced tubular sodium chloride concentration, the macula densa cells release EDRF and prostaglandins locally, which cause afferent arteriolar vasodilatation. This afferent vasodilatation results in increased blood flow and GFR."

Fig 16. Mechanism of renal response to Protein load



Utility of the protein tolerance test in clinical nephrology:

"The protein tolerance test can be utilized in:

a. Assessing the baseline and progression of renal disease in certain high risk groups –like diabetics, hypertensives, polycystic kidney disease patients, and patients with a solitary kidney. These patients can be accurately prognosticated and planned for more aggressive intervention if required, by testing with stress GFR as compared to resting GFR.

b. Assessment of borderline donors. Due to shortage of live related donors, elderly and hypertensive individuals are now being taken up as potential renal donors. Stress GFR in at least these high risk donors will be desirable to reject those who are likely to have renal compromise subsequently, though they might be having a normal resting GFR."

Procedure for conducting PTT[44] :

The protein tolerance test has two components:

1. Stress GFR
2. Tubular stress test

STRESS GFR

"As described by Bosch et al[42], Patients should be fasting and should receive oral hydration with 20 ml/kg of water. Once hydration is complete, urine volume is replaced by an equal quantity of water. Endogenous creatinine clearance is used for assessing the test and baseline GFR. Baseline GFR– Two blood samples are collected for serum creatinine measurement at the start and 30 minutes apart for calculation of creatinine clearance by Cockcroft and Gault equation (CG formula) and the mean is taken as baseline creatinine clearance."

TUBULAR STRESS TEST:

"Herrena et al [45] assessed the functional reserve of the kidney by performing tubular function. It is documented that, Increase in tubular secretion of creatinine (TScr) after a test meat meal. They demonstrated that in normal individual TScr was three times the baseline, while patients with moderate renal failure were unable to raise their TScr." However, it requires standardization and further studies needed to prove its utility.

INTERPRETATION:

In normal individuals, protein tolerance test will show an increase in GFR from baseline in absence of urinary protein. In contrast, those with abnormal test will have proteinuria and no increase in GFR. The maximal filtration capacity attained after the protein load in various western studies is reported to be around 140 -160 ml/min/1.73 m2 with a percentage increase in GFR of 20 - 40% from basal state[2, 3, 5.] Increase in GFR without any proteinuria suggests normal response, while increase in GFR with proteinuria would suggest renal injury and no increase in GFR would suggest incipient renal failure.

Hence, protein tolerance test can be used to ascertain an individual's renal reserve, with incipient renal failure even though with Normal GFR and serum creatinine. Thus, appropriate measures can be initiated at the earliest in such cases. Not much literature is available at the moment in relation to this test. In India, only two studies have evaluated the protein tolerance test and proved that protein tolerance test was a useful tool in identifying at risk patients.

MATERIALS

&

METHODS

MATERIALS AND METHODS:

This study was conducted in Government Royapettah hospital, Chennai for a duration of 6 months from April 2015 to Sep 2015. A proper ethical approval was obtained from the Institutional Ethical Committee .The study was conducted after getting informed consent from all the Subjects involved in this study.

Study Design	:	Cross Sectional Comparative Study
Collaborating Depts.	:	Diabetology, Biochemistry, And Master Health Check up
Study Period	:	6 months (April 2015 to Sep 2015)
Conflict of Interest	:	Nil

Study population:

Patients attending Diabetology outpatient department will be included in the study. An equal number of Healthy, age and sex matched subjects without diabetes or its complications, who are undergoing Master Health Check up will be included in the study for comparison.

Inclusion Criteria:

- Patients with type 2 diabetes mellitus
- Healthy, age and sex matched subjects without diabetes or its complications, who are also included in the study for comparison.

Exclusion Criteria:

- Type 2 diabetes mellitus with Proteinuria
- Systemic hypertension
- Renal Failure

Diagnosis of Type 2 diabetes mellitus was made by clinical records and blood investigations including fasting and postprandial blood glucose values. The WHO criteria were employed for the diagnosis of diabetes mellitus.[2]

The presence of absence of renal dysfunction was made on the basis of the following:

1. Clinical details
2. Investigations – Sr. Creatinine, creatinine clearance, Spot urinary protein estimation

SAMPLE SIZE: **104 (52 cases + 52 controls)**

According to this formula:

$$n = \frac{Z^2 p(1-p)}{d^2}$$

p (Prevalence of kidney disease in Type 2 Diabetes) =40%

d (absolute Precision) = 10%)

Assuming alpha error = 5%,

Methodology:

After obtaining informed written consent, basic demographic details, detailed clinical history and physical examination will be done. Base line Fasting Blood sample for Serum Creatinine, Blood Glucose and urine sample for PCR will be collected.

Then study population were subjected to a "Protein Tolerance Test" using protein meal -100 gm of protein as cottage cheese. After giving high protein meal, Blood samples were collected at 60 and 120 minutes for serum creatinine and Urine samples were collected at 120 mins for Urine PCR measurement.

To assess the Renal Functional Reserve, by e GFR was calculated by using **Cockcroft-Gault Equation**:

$$eCrCl = \frac{(140 - Age) \times Weight\ (kg)}{72 \times Creatinine_{serum\ (mg/dL)}} \times 0.85 \text{ if female}$$

INTERPRETATION OF RESULTS:

1. **Urine PCR :**
   i. Normal :- ≤ 20 mg
   ii. Abnormal :- ≥ 20 mg
2. **Renal Function:**
   i. Normal :- Increase in GFR without any proteinuria
   ii. Renal injury :- Increase in GFR with proteinuria
   iii. Renal failure :- No increase in GFR with proteinuria

DATA COLLECTION & ANALYSIS:

The data of each patient will be collected on a proforma specially designed for this study and which includes demographic details, past medical history, diabetic profile and renal functional reserve before

and after Protein Tolerance test. The information collected regarding all the selected subjects were recorded in a Master Chart.

The collected data was analyzed to identify the percentage of incipient renal failure in patients with normal GFR and normal serum creatinine in Type 2 Diabetes patients and compared with normal population by using SPSS for windows, version 16.0, Chicago Inc.

To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. The normality of the data was verified with “Shapiro Wilk's test” for normality showed the data is normal. To find the significant difference between the bivariate samples in Paired groups “Paired sample t-test” was used & for Independent groups the “unpaired sample t-test” was used. For repeated measures the “Repeated measures of ANOVA” with adjustment for multiple comparisons to control the type I error, the “Bonferroni test” was used. To find the significance in categorical data “Chi-Square test” was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

RESULTS

&

ANALYSIS

RESULTS AND STATISTICAL ANALYSIS

STUDY POPULATION:

Majority of the study subjects were from in and around Chennai city urban population. The total number of study population included in the study was 104. Among them 52 are cases and 52 controls were also included in the study for comparative analysis.

AGE DISTRIBUTION:

The age of the controls ranged from 35 to 69 years with a mean age of 51.7 years. The age of the patients in the cases ranged from 32-67 years with a mean of 53.9 years. Among the cases, 2 patients were in the age group of up to 40 years (3.8%) , 14 patients in 41-50 age group (26.9%), 29 patients in 51-60 age group (55.8%),7 patients (13.5%) were in the age group of >60years.

The age groups of the cases and controls were comparable and there was no statistical difference (p=0.089)

TABLE 6: AGE DISTRIBUTION

Age Range	Number	CASES	CONTROLS	Total
Up to 40 yrs	Count	2	9	**11**
	%	3.8%	17.3%	**10.6%**
41 - 50 yrs	Count	14	17	**31**
	%	26.9%	32.7%	**29.8%**
51 - 60 yrs	Count	29	22	**51**
	%	55.8%	42.3%	**49.0%**
Above 60 yrs	Count	7	4	**11**
	%	13.5%	7.7%	**10.6%**
Total	**Count**	**52**	**52**	**104**
"p" value - 0.089 (Not significant)				

GENDER DISTRIBUTION:

In the study population among the cases 23 are females and 29 are males and among the controls 25 are females and 27 males.

TABLE 7: GENDER DISTRIBUTION

GENDER	Number	CASES	CONTROLS	Total
Female	Count	23	25	**48**
	%	44.2%	48.1%	**46.2%**
Male	Count	29	27	**56**
	%	55.8%	51.9%	**53.8%**
Total	**Count**	**52**	**52**	**104**
"p" value - 0.694 (Not significant)				

The gender of the patients and controls were comparable and there was no statistical difference (p=0.694)

TABLE 8: Quantitative parameters

Variable	Renal Function	Number	Mean	S .D	'p' value	Significance
Age	Failure	12	59.75	5.848	**0.0001**	**Highly significant**
	Injury	9	57.89	5.278		
	Normal	31	50.52	6.678		
	Total	52	53.92	7.470		
Duration of DM in yrs	Failure	12	11	1.603	**0.0001**	**Highly significant**
	Injury	9	7	1.323		
	Normal	31	5	.995		
	Total	52	6.46	2.845		
PPBG-2hr	Failure	12	294.00	35.481	**0.0001**	**Highly significant**
	Injury	9	296.89	36.412		
	Normal	31	226.10	31.448		
	Total	52	254.02	47.282		
S.Cr (0 min)	Failure	12	.9125	.12636	**0.728**	Not Significant
	Injury	9	.8722	.16604		
	Normal	31	.9048	.10516		
	Total	52	.9010	.12025		
S.Cr (60Min)	Failure	12	1.0167	.13371	**0.001**	**Significant**
	Injury	9	.8333	.18028		
	Normal	31	.8484	.12075		
	Total	52	.8846	.15131		
S.Cr (120Min)	Failure	12	.9250	.14848	**0.0001**	**Highly significant**
	Injury	9	.7556	.16667		
	Normal	31	.6452	.10276		
	Total	52	.7288	.16959		
e GFR1	Failure	12	69.7667	8.96028	**0.466**	Not Significant
	Injury	9	70.9911	7.45399		
	Normal	31	73.0787	8.13799		
	Total	52	71.9531	8.18826		
e GFR 2	Failure	12	65.9433	10.34144	**0.0001**	**Highly significant**
	Injury	9	77.5778	9.64677		
	Normal	31	88.3065	11.57919		
	Total	52	81.2888	14.29358		
Mean S.Cr1	Failure	12	.9125	.12636	**0.728**	Not Significant
	Injury	9	.8722	.16604		
	Normal	31	.9048	.10516		
	Total	52	.9010	.12025		
Mean S.Cr2	Failure	12	.9708	.13561	**0.0001**	**Highly significant**
	Injury	9	.8000	.15811		
	Normal	31	.7484	.08610		
	Total	52	.8087	.14373		

BMI :

Study population were classified as overweight(≥25), normal weight(18.5-24.5) and underweight(≤18.5) according to the Body Mass index(kg/m^2).Out of 52 controls, 13 were in the underweight group(25%), 27 were in the normal weight group (51.9%) and12 were (23.1 %) in the overweight group. Out of 52 cases, 14 were in the underweight group (26.9%) were in, 25 were in the normal weight group (48.1%) and 13 were in the overweight group (25%).

TABLE 9: BMI and Study Population

BMI	Number	CASES	CONTROLS	Total
Normal	Count	25	27	**52**
	%	48.1%	51.9%	**50.0%**
Over weight	Count	13	12	**25**
	%	25.0%	23.1%	**24.0%**
Under weight	Count	14	13	**27**
	%	26.9%	25.0%	**26.0%**
Total	**Count**	**52**	**52**	**104**
"p" value - 0.926 (Not significant)				

The mean height, weight and BMI of the patients and controls were comparable and there was no statistical difference (p values are 0.907, 0.834 & 0.926 respectively).

BLOOD GLUCOSE:

Fasting (0 hr) and postprandial (2 hrs) blood glucose values were analyzed in the two groups. The mean FPG in control group was 90.4 mg/dl compared to 155.6 mg/dl in the cases. On the other hand mean 2 hour PPG values in control group were 129.1mg/dl as opposed to 254.1mg/dl in the cases.

Both the Fasting and Post prandial Blood Glucose values of the cases and controls were comparable and statistically significant (p values are 0.0001 & 0.0001 respectively)

SERUM CREATININE:

Serum creatinine @0 min and post protein load Serum creatinine levels @ 60, 120 min & mean were analyzed. The Serum creatinine @ 0 min values were 0.86 mg/dl in control group, 0.90 mg/dl in cases group. The difference between the two groups was statistically not significant (p=0.079).

The mean post protein load Serum creatinine @ 60 min and 120 min values were 0.76mg/dl and 0.65 mg/dl in control group, 0.88mg/dl and 0.73 mg/dl in the cases group respectively. **The difference between the two groups was statistically significant (p values are 0.0001 & 0.005 respectively)**

The post protein load mean Serum creatinine values were 0.7 mg/dl in control group, 0.81 mg/dl in cases group. **The difference between the two groups was statistically significant (p=0.0001).**

e-GFR :

The e GFR-1 mean value was 76.83 in the control group compared to 71.95 in the cases .**The difference between the two groups was** statistically **significant (p=0.016).**

The e GFR-2 values remained persistently decreased with a mean of 95.38 in the control group compared to 81.28 in the study group .**The difference between the two groups was statistically significant (p=0.0001).**

Urine Protein Creatinine Ratio (PCR):

Urine PCR was analyzed in the two groups at 0 min and 120 min after protein meal .The results are summarized in table 4 & 5.

TABLE 10: Urine PCR 0 min and Study Population

Urine PCR (0 min)	CASES	CONTROLS	Total
Abnormal	0	0	**0**
Normal	52	52	**104**
Total	**52**	**52**	**104**

TABLE 11: Urine PCR @120 min and Study Population:

Urine PCR (120 min)	Number	CASES	CONTROLS	Total
Abnormal	Count	21	2	**23**
	%	40.4%	3.8%	**22.1%**
Normal	Count	31	50	**81**
	%	59.6%	96.2%	**77.9%**
Total	**Count**	**52**	**52**	**104**
"p" value - 0.0001 (Highly significant)				

Urine PCR was normal @ 0 min in the both the groups. **Urine PCR @120 min was higher (Abnormal) in the cases group than the control group, which was statistically significant (p=0.0001).**

RENAL FUNCTION ANALYSIS:

Renal function was analyzed in the two groups. Normal Renal Function was observed in 50 patients (96.2%) in the control group compared to 31 patients (59.6%) in the cases. Renal injury was observed in 2 patients (3.8%) in the control group compared to 9 patients (17.3%) in the cases group**.** Renal Failure was observed in none of the patients in the control group compared to 12 patients (23.1%) in the cases group**. The prevalence of Renal dysfunction was more in the study group (40.4%) compared to 3.8 % in controls and the difference was statistically significant (p=0.0001).** The results are shown in table 6.

TABLE 12: RENAL FUNCTION

Renal Function	Number	CASES	CONTROLS	Total
Failure	Count	12	0	**12**
	%	23.1%	0.0%	**11.5%**
Injury	Count	9	2	**11**
	%	17.3%	3.8%	**10.6%**
Normal	Count	31	50	**81**
	%	59.6%	96.2%	**77.9%**
Total	**Count**	**52**	**52**	**104**
"p" value - 0.0001 (Highly significant)				

AGE AND RENAL FUNCTION:

The relation between age and renal function was analyzed. It was found that renal failure was more in patients over 60 years (50%) as compared to 41.7% in the 51-60 years group, 8.3% in the 41-50 years group and none in the < 40yrs of age. **The difference was found to be statistically significant (p=0.001).**

TABLE 13: AGE AND RENAL FUNCTION

Age Range	Number	Renal Function			Total
		Failure	Injury	Normal	
Up to 40 yrs	Count	0	0	2	**2**
	%	0.0%	0.0%	6.5%	**3.8%**
41 - 50 yrs	Count	1	1	12	**14**
	%	8.3%	11.1%	38.7%	**26.9%**
51 - 60 yrs	Count	5	7	17	**29**
	%	41.7%	77.8%	54.8%	**55.8%**
Above 60 yrs	Count	6	1	0	**7**
	%	50.0%	11.1%	0.0%	**13.5%**
Total	**Count**	**12**	**9**	**31**	**52**
"p" value - 0.001 (Highly significant)					

SEX AND RENAL FUNCTION:

The relation between sex and renal function was analyzed. It was found that renal failure was more in patients in males (58.3%) as compared to 41.7% in the females and injury also more in patients in males (55.3%) as compared to 44.4% in the females .But the difference was not statistically significant (p=0.979)

TABLE 14: SEX AND RENAL FUNCTION

SEX	Number	Renal Function			Total
		Failure	Injury	Normal	
Female	Count	5	4	14	23
	%	41.7%	44.4%	45.2%	44.2%
Male	Count	7	5	17	29
	%	58.3%	55.6%	54.8%	55.8%
Total	**Count**	**12**	**9**	**31**	**52**
"p" value - 0.979 (Not significant)					

BMI AND RENAL FUNCTION:

TABLE 15: BMI AND RENAL FUNCTION:

BMI	Number	Renal Function			Total
		Failure	Injury	Normal	
Normal	Count	6	3	16	**25**
	%	50.0%	33.3%	51.6%	**48.1%**
Overweight	Count	4	3	6	**13**
	%	33.3%	33.3%	19.4%	**25.0%**
Underweight	Count	2	3	9	**14**
	%	16.7%	33.3%	29.0%	**26.9%**
Total	**Count**	**12**	**9**	**31**	**52**
"p" value – 0.711 (Not significant)					

DURATION OF DISEASE AND RENAL FUNCTION:

The relation between duration of disease and renal dysfunction was analyzed. It was seen that 7 out of 12 patients (58.3%) with a longer duration of disease (>10 years) had renal failure compared to 5 out of 13 patients (41.7%) with duration of disease between 5-10 years. None of the patients with duration of disease <5 years had renal failure**.** The values are summarized in table 10. **The difference was found to be statistically significant (p=0.0001).**

TABLE 16: DURATION OF DISEASE AND RENAL FUNCTION

Duration of DM	**Number**	**Renal Function**			**Total**
		Failure	**Injury**	**Normal**	
< 5 yrs	Count	0	0	14	**14**
	%	0.0%	0.0%	45.2%	**26.9%**
5 - 10 yrs	Count	5	9	17	**31**
	%	41.7%	100.0%	54.8%	**59.6%**
> 10 yrs	Count	7	0	0	**7**
	%	58.3%	0.0%	0.0%	**13.5%**
Total	**Count**	**12**	**9**	**31**	**52**
"p" value - 0.0001 (Highly significant)					

URINE PCR AND RENAL FUNCTION:

Analysis was done in relation to urine PCR and renal dysfunction. It was found that abnormal urine PCR was seen in 21 patients at 120 minutes compared to none at 0 minutes. 12 out of these 21 patients had renal failure and 9 out of 21 patients had renal injury. The results are presented in the following table 11. **The difference was found to be statistically significant (p=0.0001).**

TABLE 17: URINE PCR AND RENAL FUNCTION

Urine PCR (120 min)	**Number**	**Renal Function**			**Total**
		Failure	**Injury**	**Normal**	
Abnormal	Count	12	9	0	**21**
	%	100.0%	100.0%	0.0%	**40.4%**
Normal	Count	0	0	31	**31**
	%	0.0%	0.0%	100.0%	**59.6%**
Total	**Count**	**12**	**9**	**31**	**52**
"p" value - 0.0001 (Highly significant)					

QUANTITATIVE PARAMETERS AND RENAL FUNCTION:

The results of Quantitate parameters and Renal Function are summarized in the following table 12.

Table 18: QUANTITATIVE PARAMETERS AND RENAL FUNCTION

Variable	Renal Function	Number	Mean	S .D	'p' value	Significance
Age	Failure	12	59.75	5.848	**0.0001**	**Highly significant**
	Injury	9	57.89	5.278		
	Normal	31	50.52	6.678		
	Total	52	53.92	7.470		
Duration of DM in yrs	Failure	12	11	1.603	**0.0001**	**Highly significant**
	Injury	9	7	1.323		
	Normal	31	5	.995		
	Total	52	6.46	2.845		
PPBG-2hr	Failure	12	294.00	35.481	**0.0001**	**Highly significant**
	Injury	9	296.89	36.412		
	Normal	31	226.10	31.448		
	Total	52	254.02	47.282		
S.Cr (0 min)	Failure	12	.9125	.12636	**0.728**	Not Significant
	Injury	9	.8722	.16604		
	Normal	31	.9048	.10516		
	Total	52	.9010	.12025		
S.Cr (60Min)	Failure	12	1.0167	.13371	**0.001**	**Significant**
	Injury	9	.8333	.18028		
	Normal	31	.8484	.12075		
	Total	52	.8846	.15131		
S.Cr (120Min)	Failure	12	.9250	.14848	**0.0001**	**Highly significant**
	Injury	9	.7556	.16667		
	Normal	31	.6452	.10276		
	Total	52	.7288	.16959		
e GFR1	Failure	12	69.7667	8.96028	**0.466**	Not Significant
	Injury	9	70.9911	7.45399		
	Normal	31	73.0787	8.13799		
	Total	52	71.9531	8.18826		
e GFR 2	Failure	12	65.9433	10.34144	**0.0001**	**Highly significant**
	Injury	9	77.5778	9.64677		
	Normal	31	88.3065	11.57919		
	Total	52	81.2888	14.29358		
Mean S.Cr1	Failure	12	.9125	.12636	**0.728**	Not Significant
	Injury	9	.8722	.16604		
	Normal	31	.9048	.10516		
	Total	52	.9010	.12025		
Mean S.Cr2	Failure	12	.9708	.13561	**0.0001**	**Highly significant**
	Injury	9	.8000	.15811		
	Normal	31	.7484	.08610		
	Total	52	.8087	.14373		

CHARTS:

Chart 1. Gender Distribution

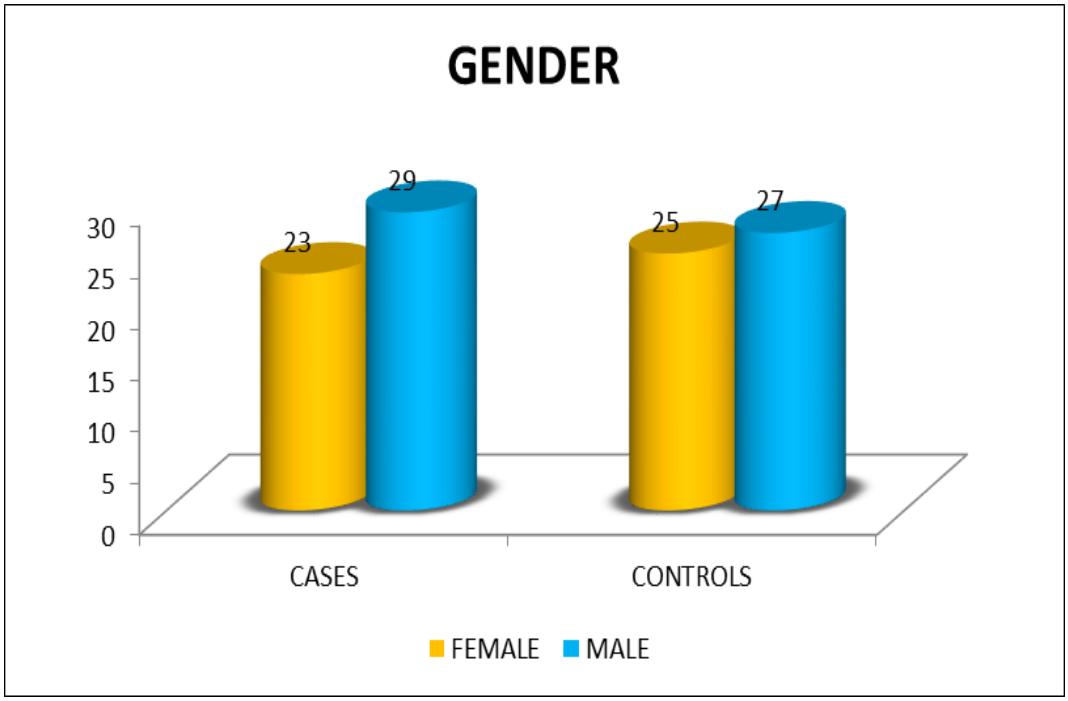


Chart 2. Age Distribution

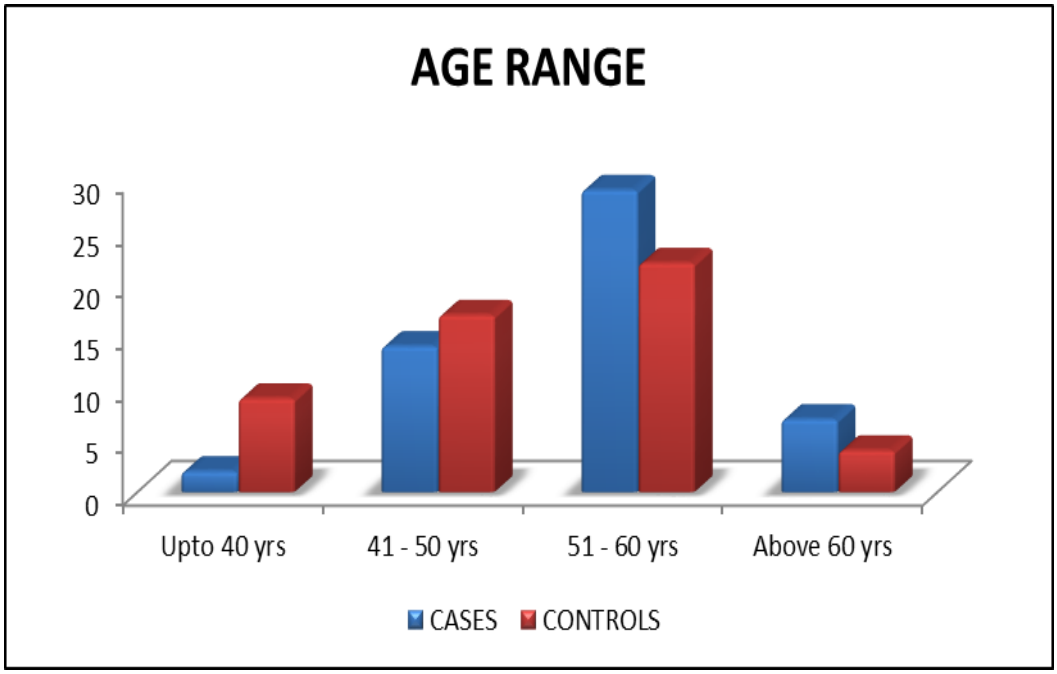


Chart 3. Weight in study population:

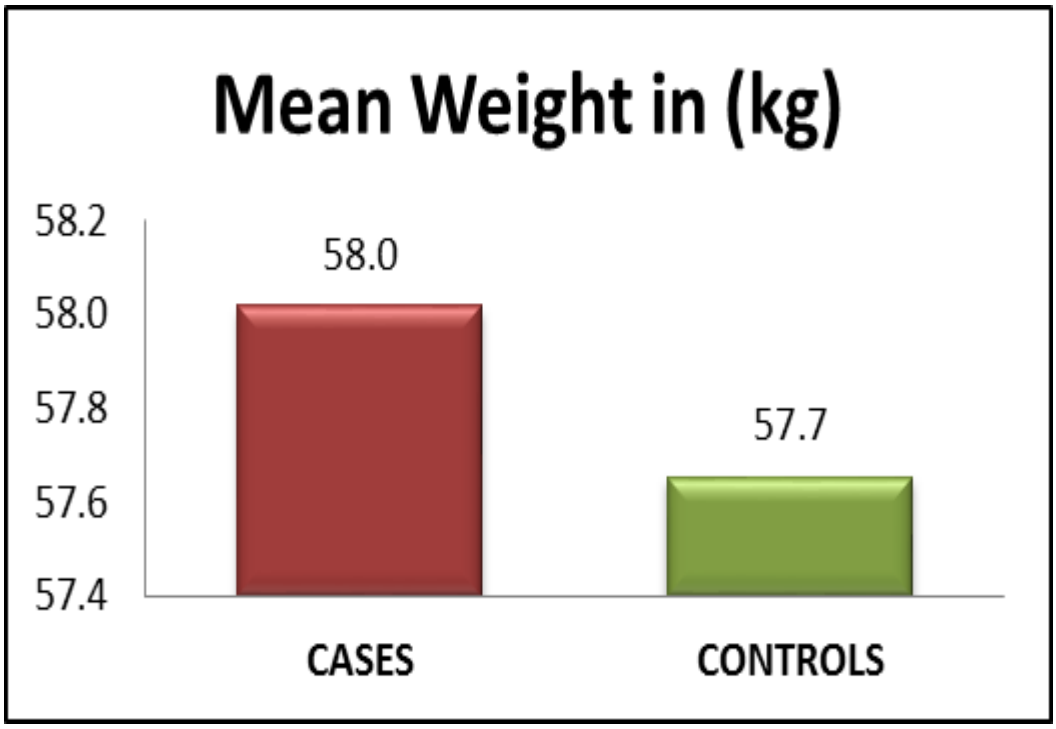


Chart 4. BMI in study population:

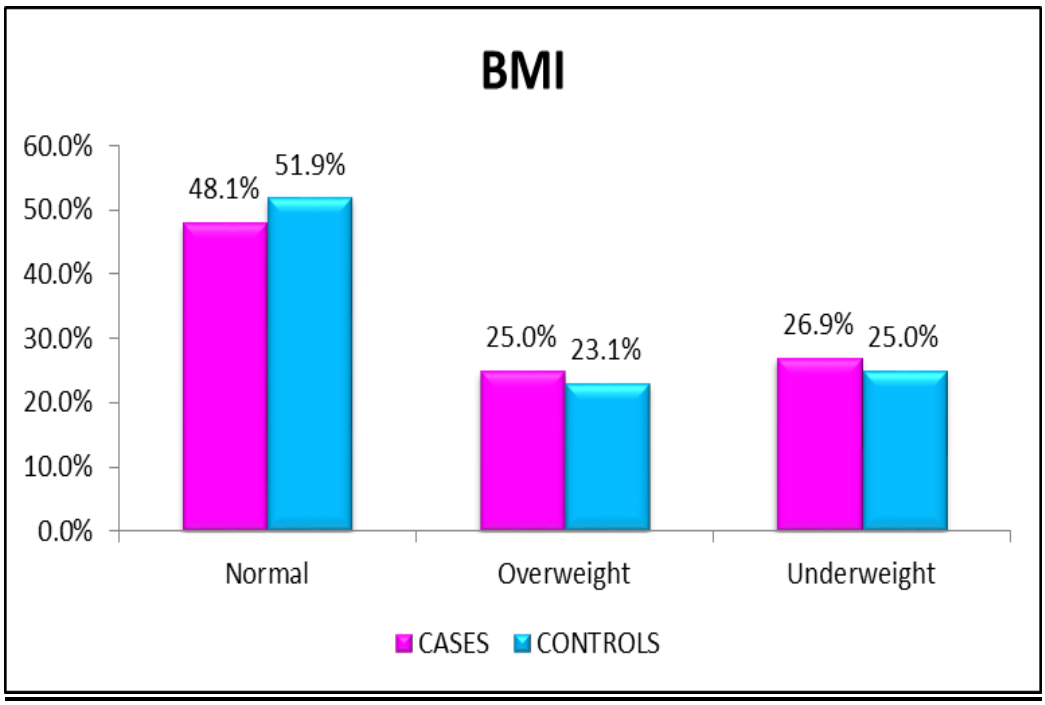


Chart 5. Fasting blood Glucose levels in study population:

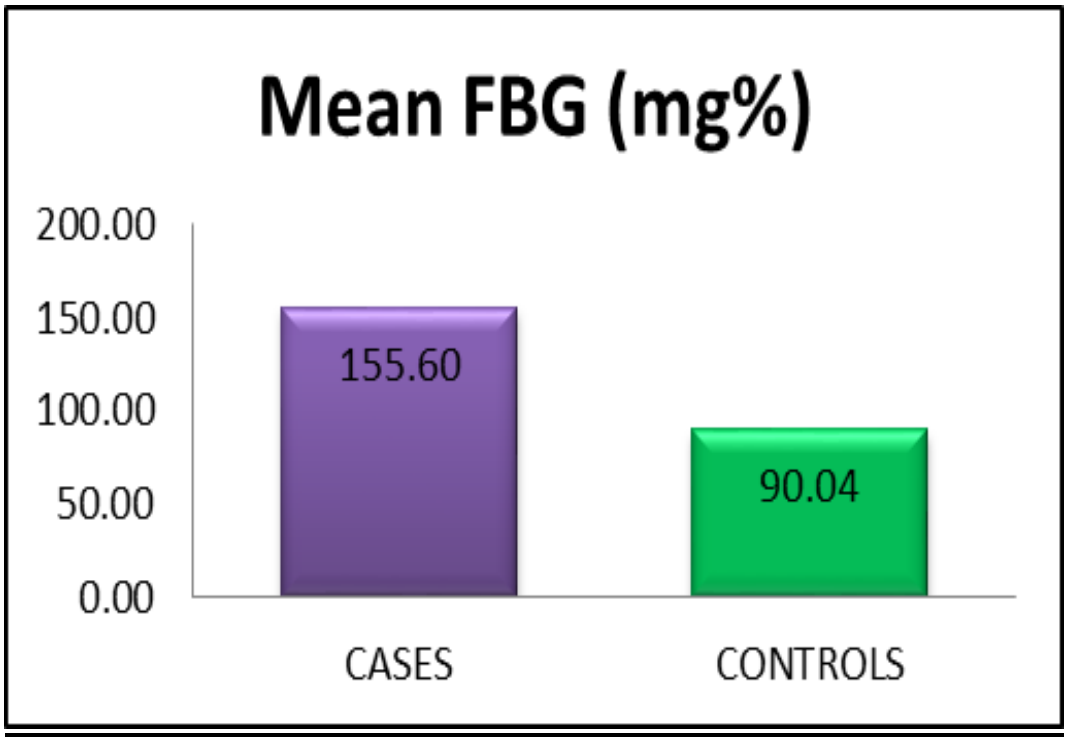


Chart 6 .Post prandial blood Glucose levels in study population:

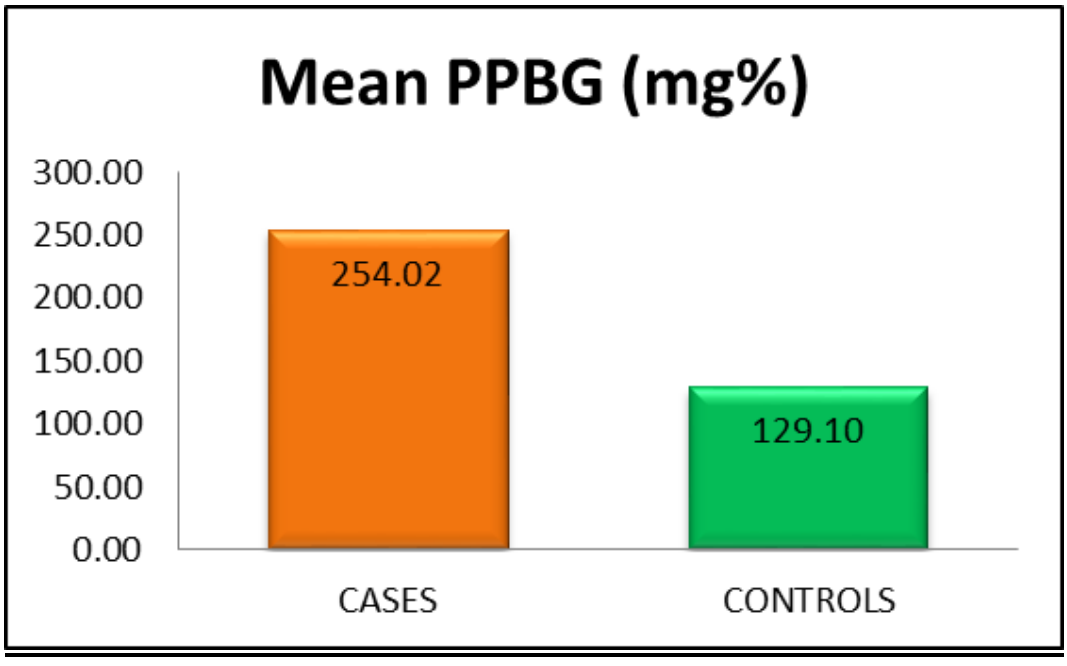


Chart 7. Serum Creatinine levels in study population:

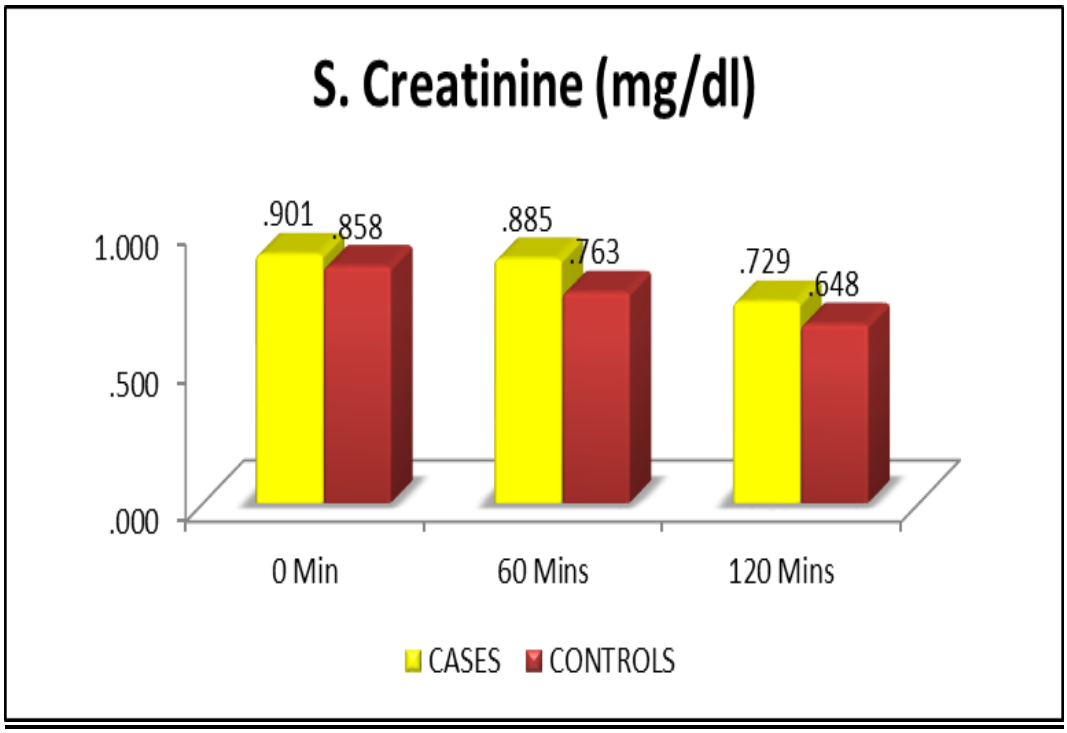


Chart 8 .e-GFR levels in study population:

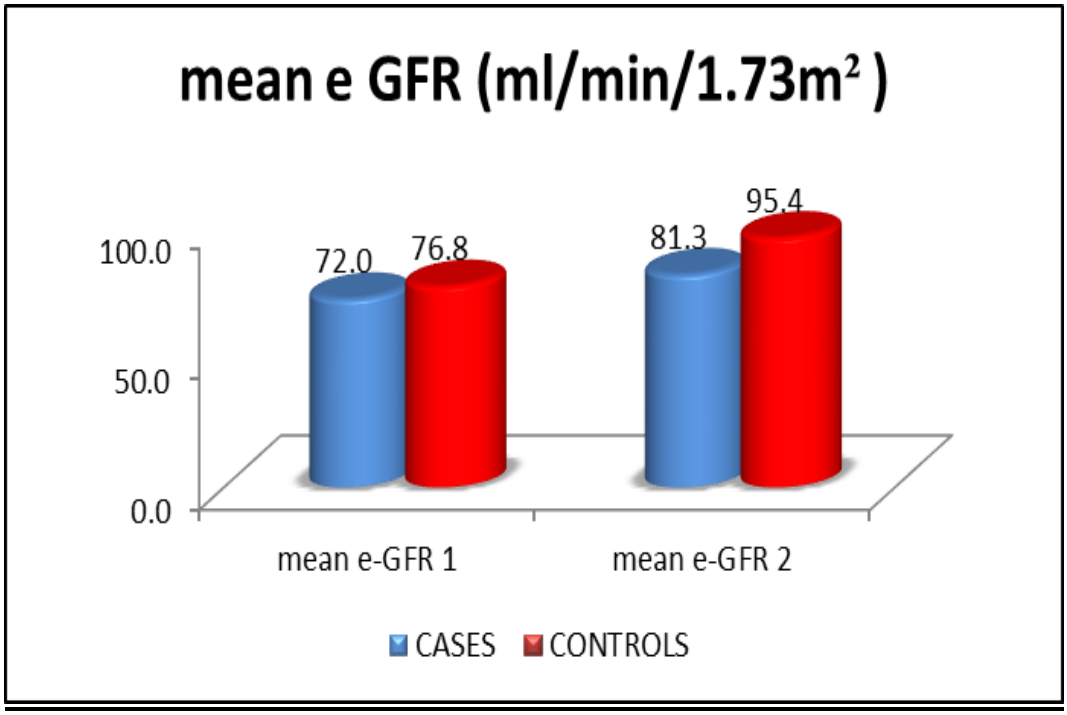


Chart 9. Urine PCR levels in study population:

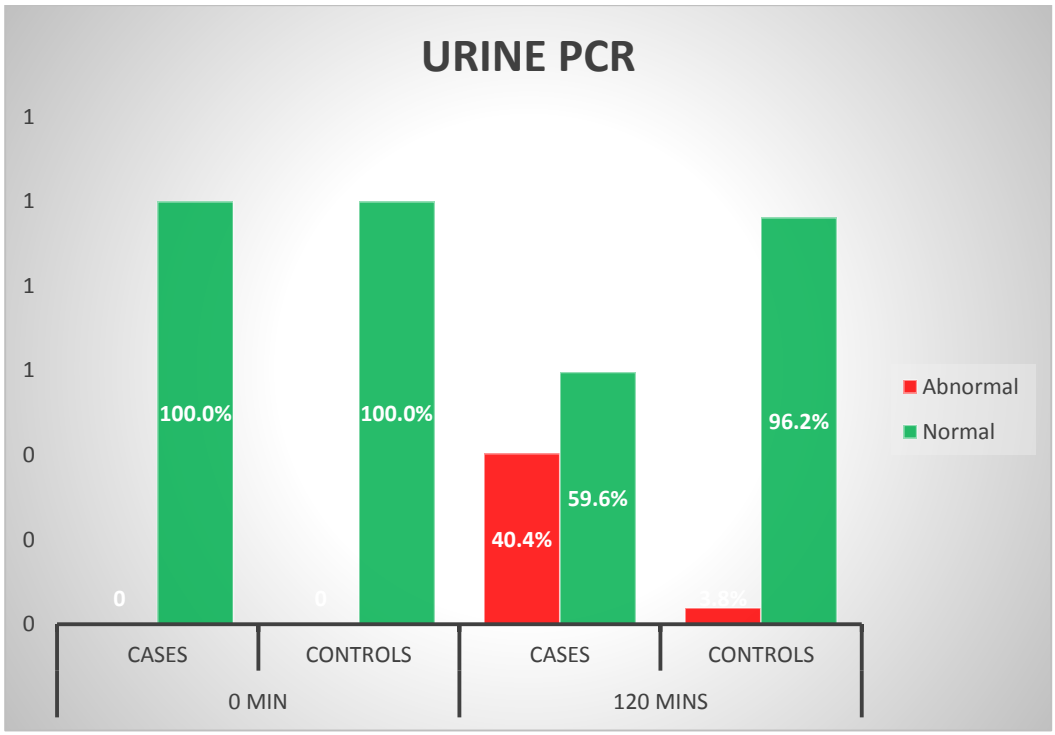


Chart 10 .Renal function in study population:

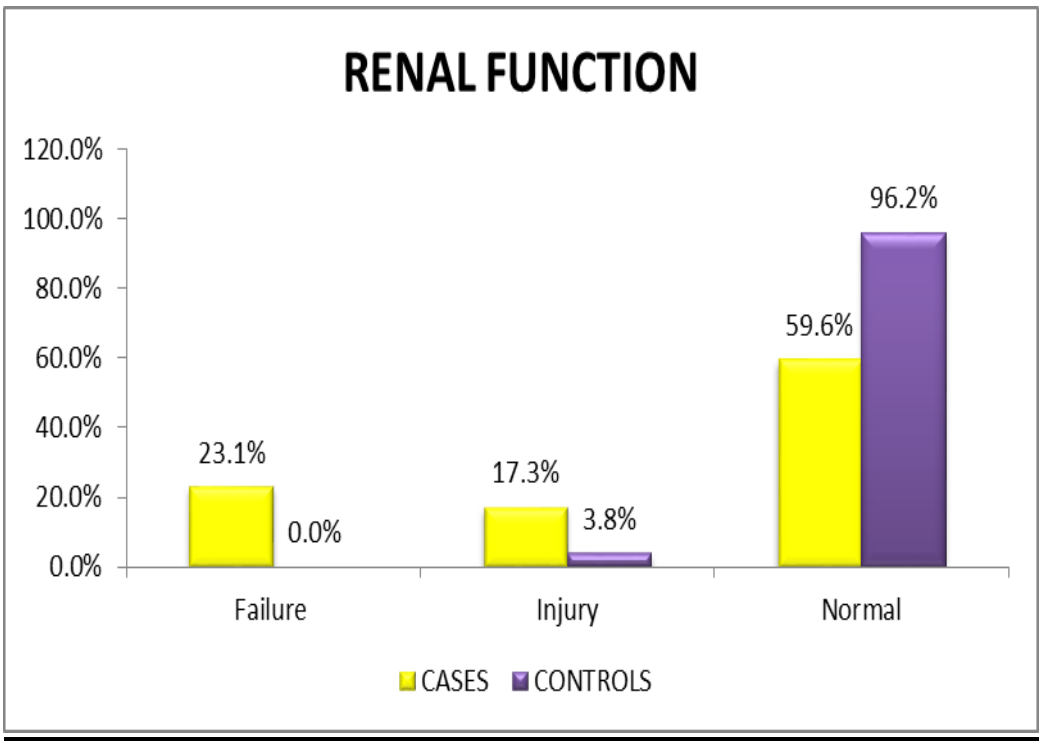


Chart 11.Renal function in cases

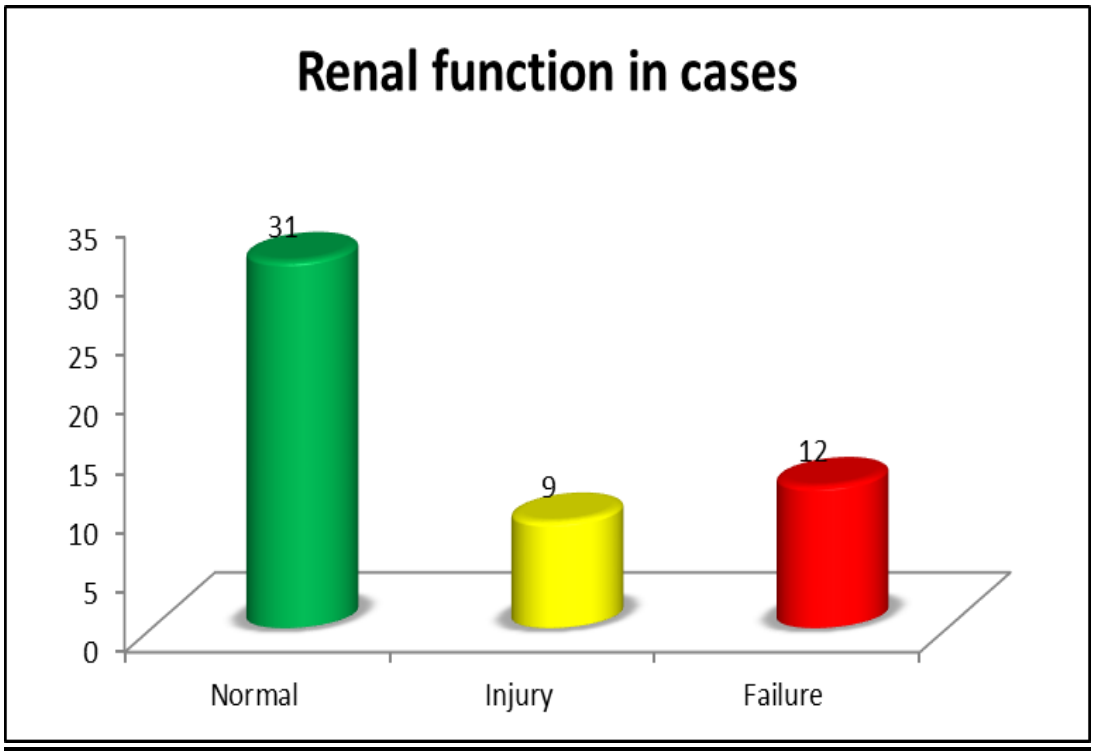


Chart 12. BMI and Renal function in cases

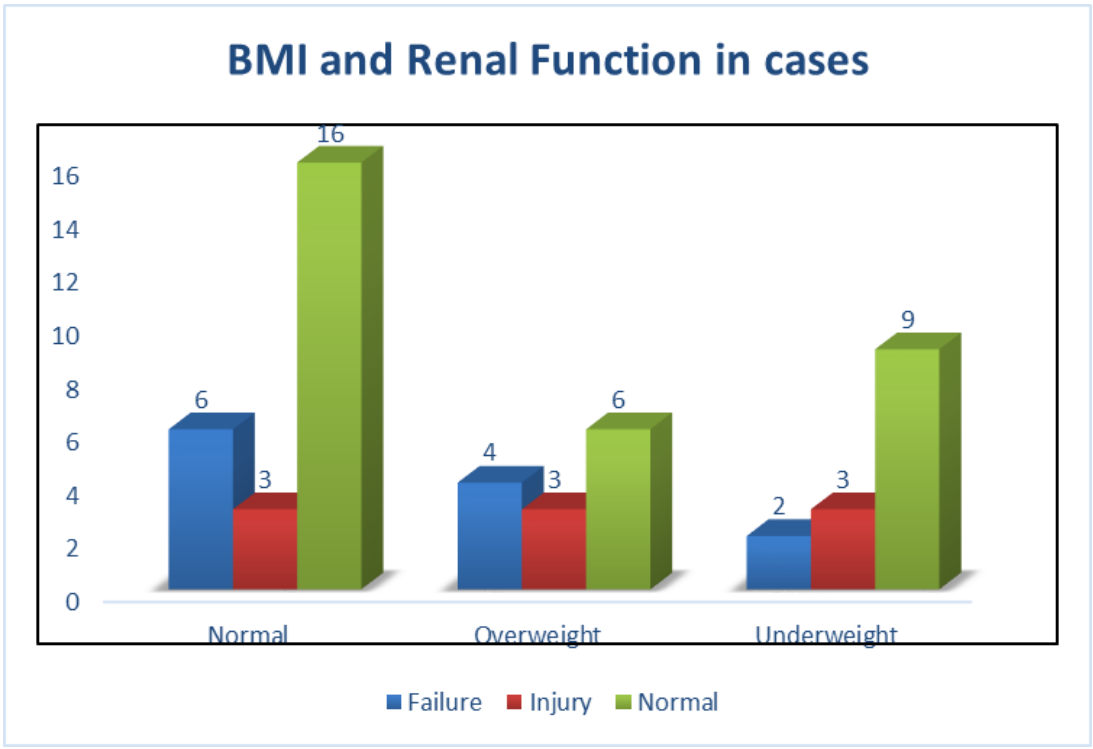


Chart 13. Gender and Renal function in cases

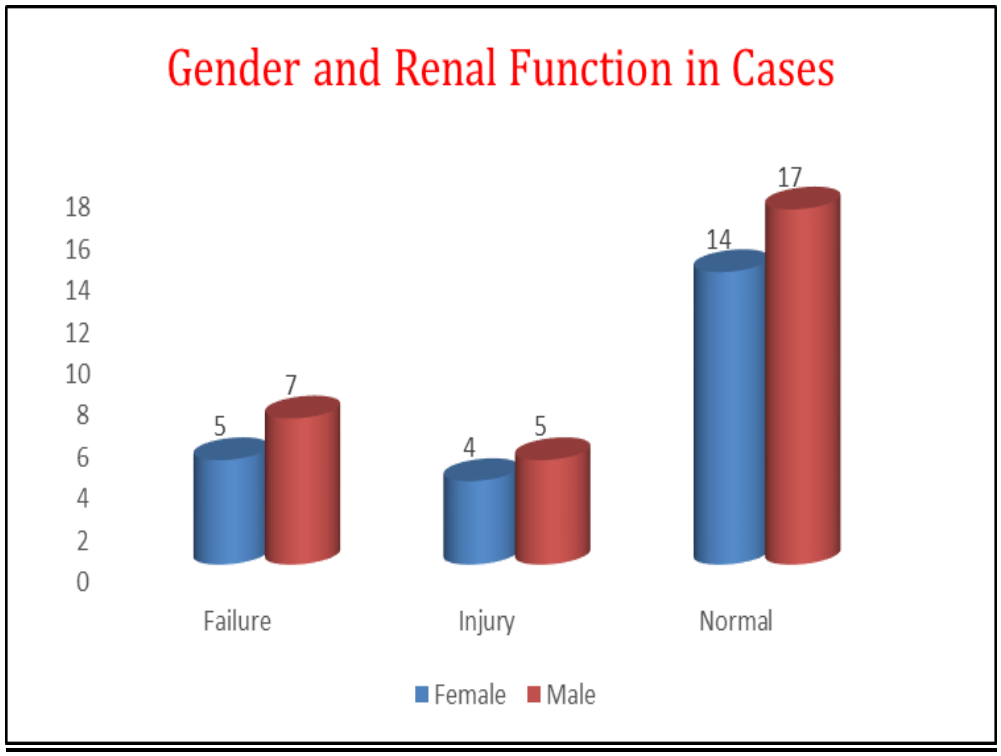


Chart 14. Age and Renal function in cases

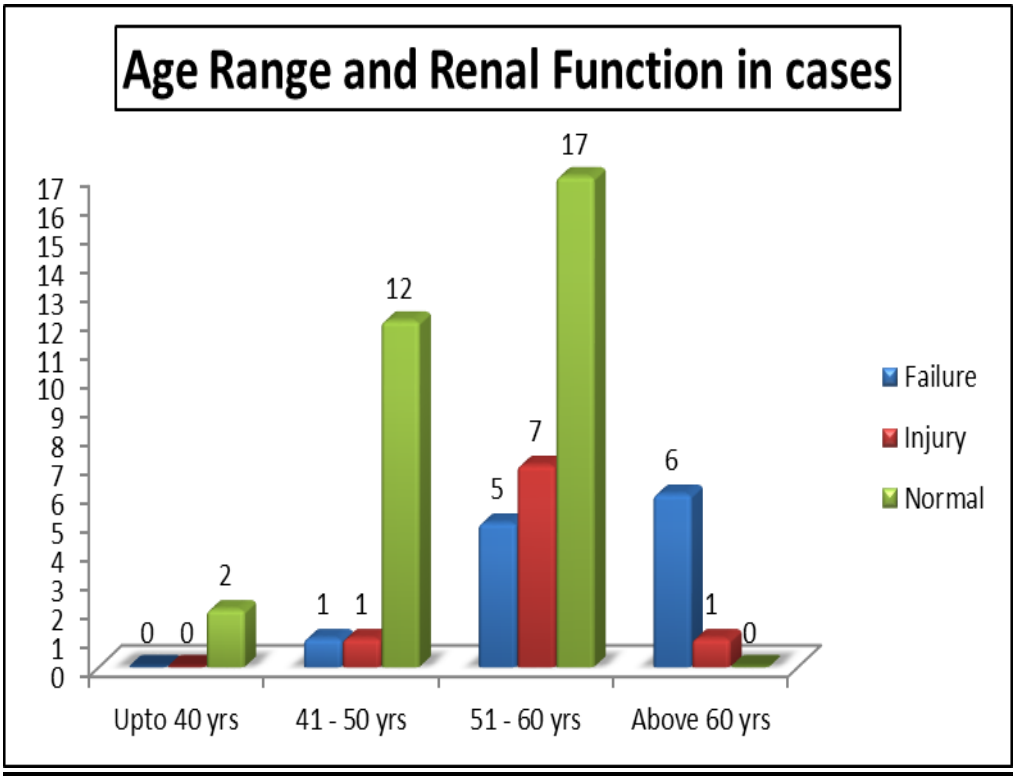


Chart 15. Duration of DM and Renal function in cases

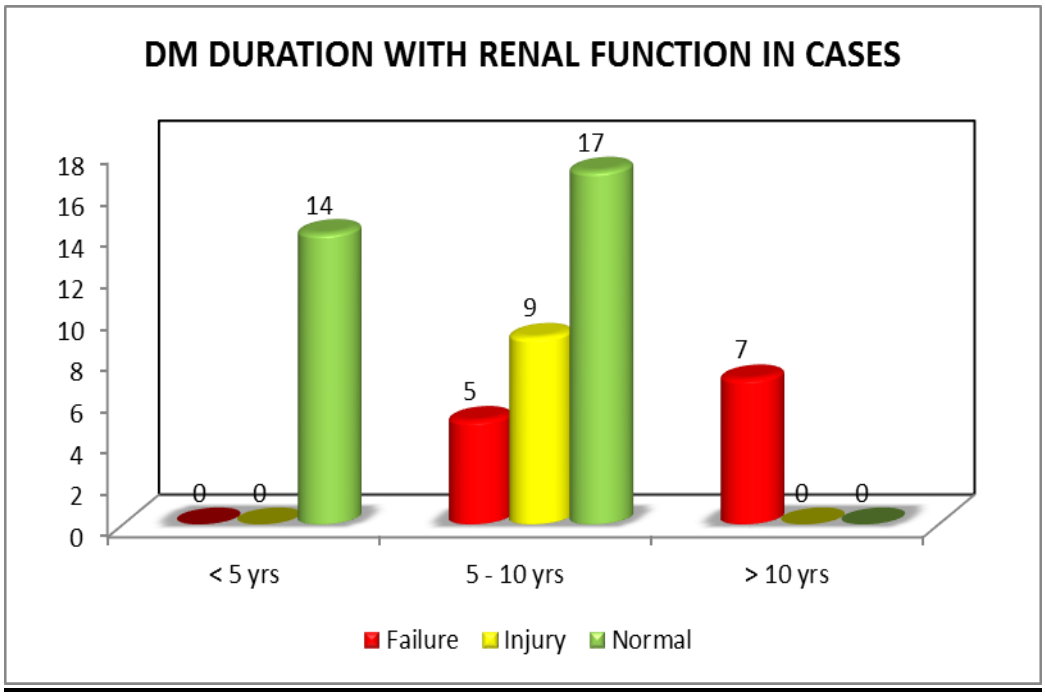


Chart 16. Urine PCR and Renal function in cases

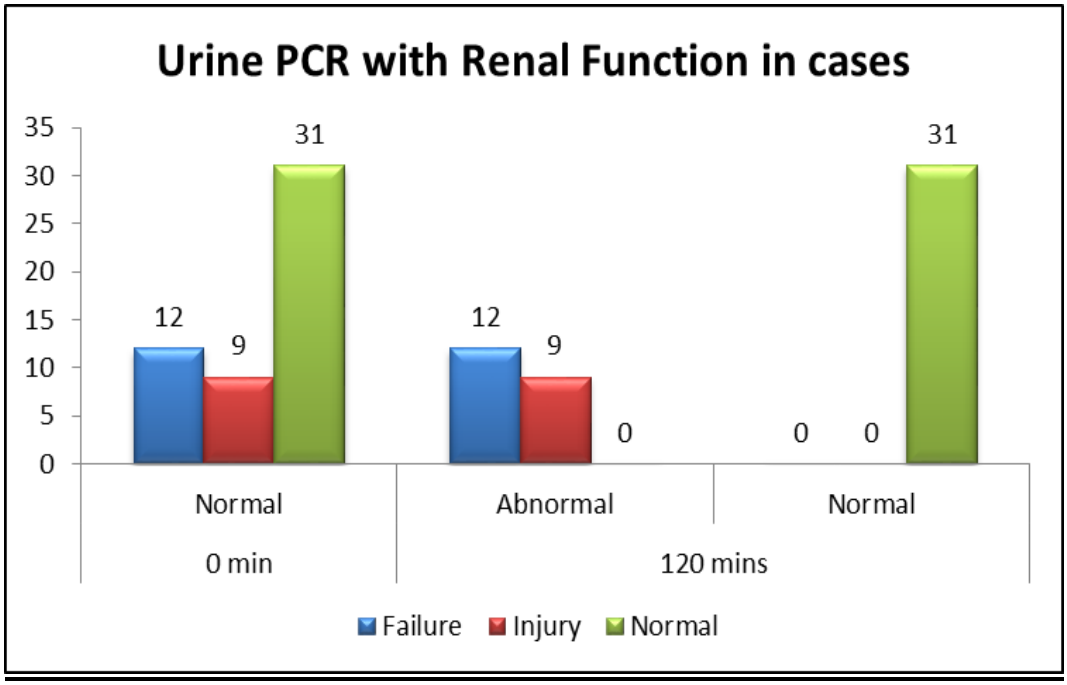


Chart 17. Sr. Creatinine and Renal function in cases

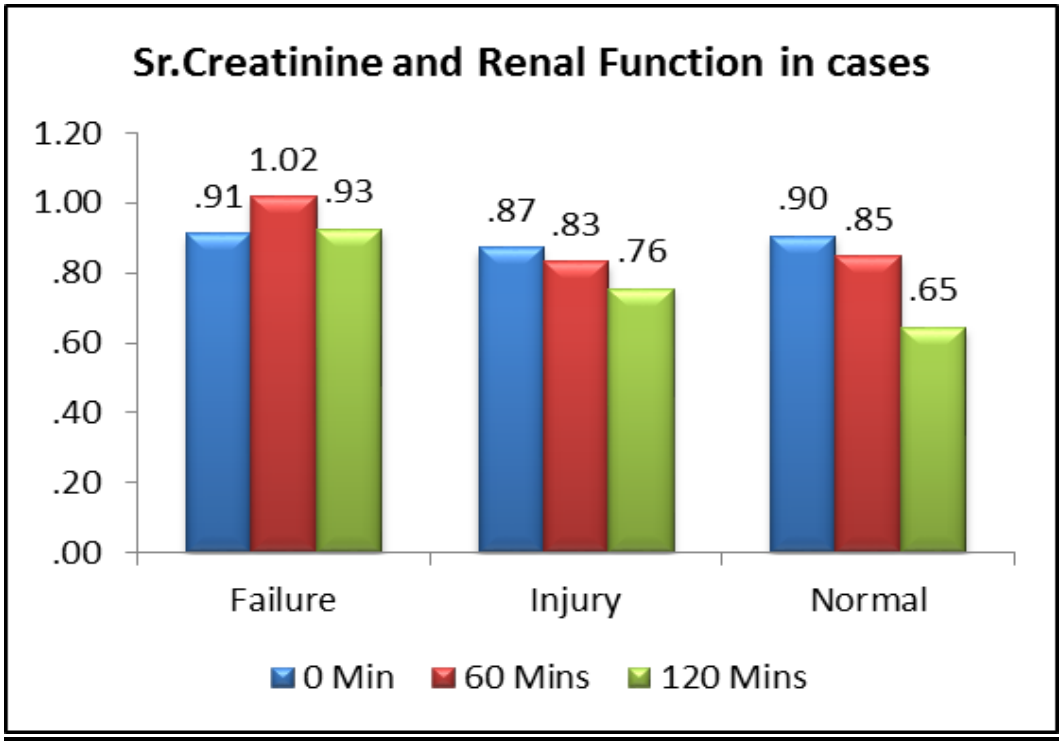
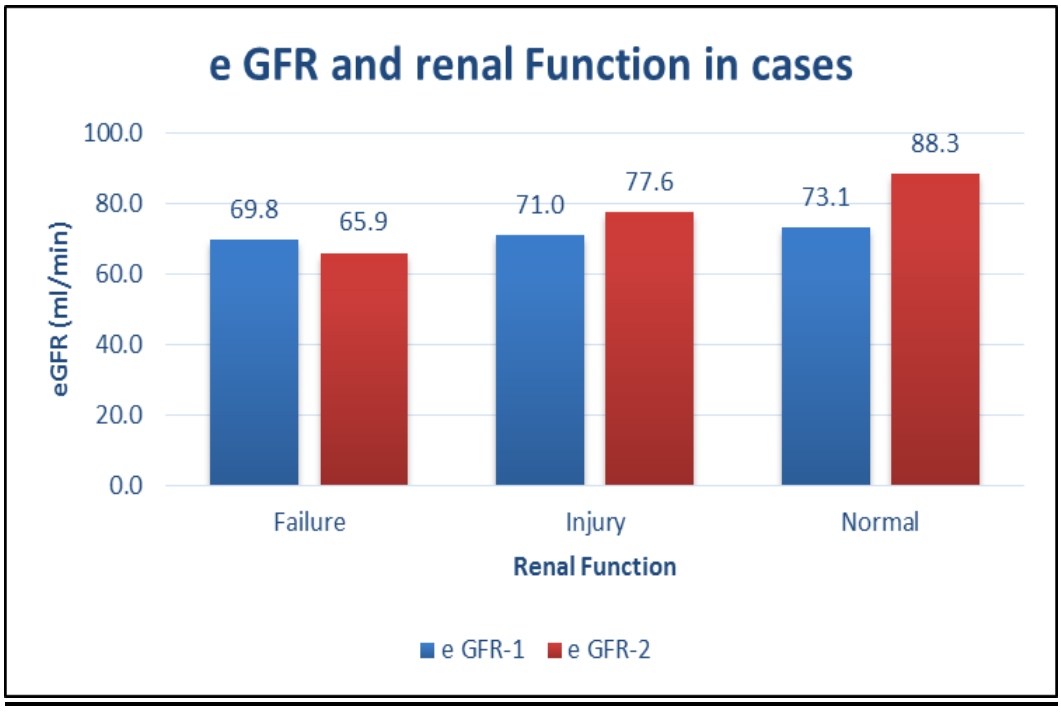


Chart 18.e-GFR and Renal function in cases



DISCUSSION

DISCUSSION

Diabetes remains a common menace in the developing population and the number has been increasing at an alarming rate in the recent years. The key to successful prevention of complications lies in early diagnosis and control. “The United Kingdom Prospective Diabetes Study, conducted from 1976 to 1997, showed conclusively that, in people with improved blood glucose control, the risk of early kidney disease was reduced by a third.” Several studies conducted over the past decades have clearly do that, “any intervention resulting in sustained lowering of blood glucose levels will be beneficial to patients in the early stages of CKD.”

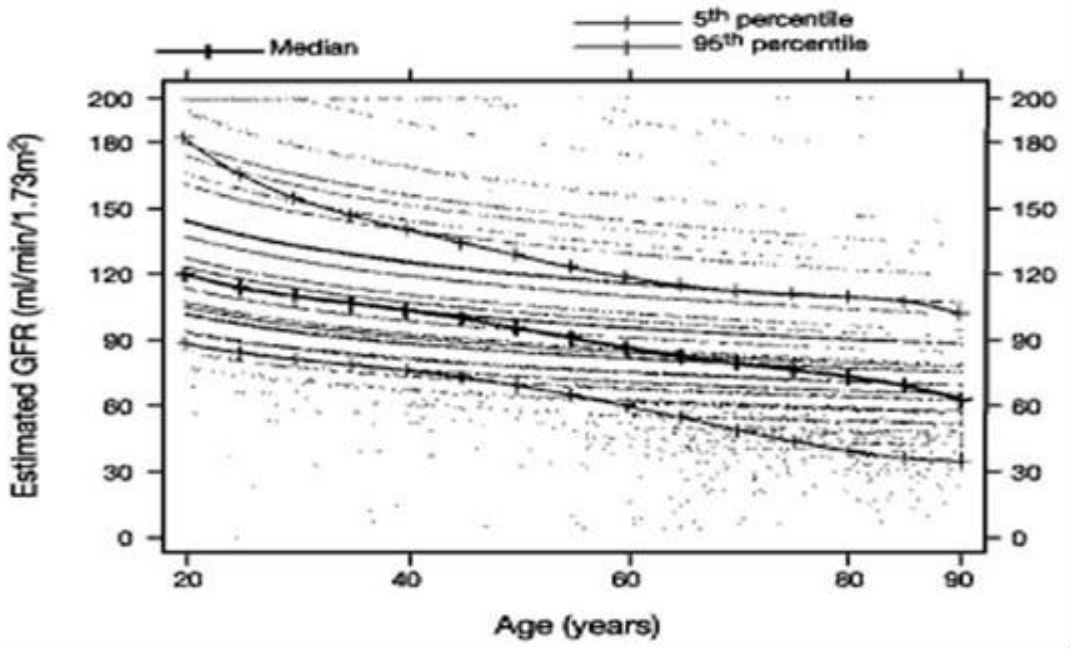
Despite adequate control of diabetes, patients may land up with one or more of the macro vascular or micro vascular complications. Diabetic nephropathy is a common problem and it remains one of the challenges for us to find the renal dysfunction at an initial stage. Early diagnosis of renal dysfunction in diabetic patients would allow us to initiate Reno protective measures at an early to prevent the progression of kidney disease and decrease the morbidity and mortality.

The early diagnosis of renal dysfunction is a challenge because the renal system has considerable functional reserve so that

routine biochemical tests for renal function can only detect abnormalities once more than 66% of functioning renal tissue has been lost. Precise evaluation of renal function would also allow more effective monitoring of the rate of decline of renal function over time and help determine the efficacy of a therapeutic intervention.

Many of the results in this study correlated well with literature. There was an age related decline in GFR similar to that seen in most studies in the past. Around 85% of patients in this study above 60 years had renal failure compared to only 13% in age group <60 years. The following graph shows the age related decline in GFR as studied in the MDRD study. This was as a result of natural history of renal disease as well as increase in conditions like diabetes and hypertension

Fig 17. Age-associated decline in estimated GFR



It was found in our study that increase in duration of diabetes was strongly related to renal failure. This is well in concurrence with the study done by coulhon et al where it was seen that “advancing age and duration of diabetes were associated with renal failure in Type 2 and Type 1 diabetes. In Type 2 diabetes duration of diabetes was a more important risk factor than age.”

In the same study, diabetic retinopathy and proteinuria were strongly associated with renal failure in both Type I and Type II diabetes mellitus. This was also seen in our study where 57% of patients with abnormal urine PCR had renal failure.

The protein tolerance test is an upcoming investigation and has not been extensively evaluated in the past. Very few studies have utilized this test to identify patients at risk of renal dysfunction.

Protein tolerance test was developed way back in 1950 by Horn et al where they proved that PTT could identify early onset diabetic nephropathy based on the fact that protein loading could exert a stress on both the glomeruli and tubules. Subsequently no major study has been done with regard to PTT. In this study it was seen that the mean creatinine- 2 values (post protein challenge) were more in patients with

renal failure compared to those with renal dysfunction and normal renal function. The decline in eGFR-2 (post protein challenge) was also statistically significant (65.9 in renal failure versus 88.3 in normal renal function) implying that this could be a useful marker of renal reserve. Though there are no major studies for comparison, the results of the study were quite significant statistically. This can be done on a larger scale to prove the utility of the protein tolerance test.

Protein tolerance test may be very useful test to diagnose the incipient renal failure in a person with normal serum creatinine and creatinine clearance and these patients who are most likely to be benefited by an early aggressive intervention. This is more important in evaluating in persons with high risk factors like hypertension, diabetes mellitus, polycystic kidney disease and post- renal transplants. PTT can also be used to check the borderline renal donor, and to give accurate prognostication in a progressive renal disease. Tubular stress test still requires standardization and further studies need to prove its utility.

SUMMARY

The study on **"Assessment of Renal Functional Reserve by Protein Tolerance Test in Type 2 Diabetes Mellitus"** was undertaken to find out the usefulness of protein tolerance test in detecting patients with type 2 diabetes mellitus who were at risk of developing renal dysfunction.

The present study was a cross sectional comparative study done at Govt. Royapettah Hospital Chennai. After institutional Ethical Committee clearance, 52 patients with type 2 diabetes mellitus and 52 healthy controls were selected according to the inclusion criteria. There were almost equal males and females in the study. A baseline fasting and post prandial blood sugar, urine PCR ,serum creatinine and baseline GFR was calculated. This was followed by a protein challenge with 100 grams of protein food. Serum creatinine and GFR were measured at 60 and 120 minutes after protein challenge.

Using statistical data, correlation was analyzed between pre/post protein challenge serum creatinine in cases and controls in relation to GFR and renal function. It was found that patients with renal failure had more persistent elevation of serum creatinine and sustained decrease in GFR as compared to patients with normal renal function or those with mild renal dysfunction. There was also an age related decline in

renal function. Proteinuria was found to be an independent risk factor for renal failure.

It was also found that patients with long duration of diabetes and poor glycaemic control have more chance of early renal injury and dysfunction than those with short duration of diabetes and good glycaemic control.

CONCLUSION

CONCLUSIONS

1. Renal damage starts in Diabetic patients even before microalbuminuria and clinical nephropathy starts.

2. It was found that longer the Duration of diabetes, more the chance of renal injury and dysfunction.

3. Renal injury and dysfunction directly correlates with poor metabolic control.

4. Protein tolerance test may be a very helpful test to diagnose occult renal failure in patients with normal serum creatinine and normal GFR values.

5. Identifying those patients with subnormal renal function may enable us to initiate an early aggressive intervention.

6. This Protein Tolerance Test may be very much useful in high risk patients like Diabetics, Hypertensive patients.

7. Patients with diseases like solitary kidney, polycystic kidney disease, post renal transplants can also be subjected to this test to identify incipient renal failure.

8. Protein Tolerance Test can also be used to check the borderline renal donor in order to give accurate prognostication in a progressive renal disease.

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ANNEXURE

MASTER CHART (Page 1 out 5)

S.NO	ID	Age in yrs	sex	weight (kg)	height (cms)	BMI (Kg/M²)	FBG (mg%)	PPBG-2hr (mg%)	Duration of DM in yrs	S.Cr (0 min) (mg%)	Mean S.Cr1 (mg%)	e GFR1 (mL/min)	S.Cr (60Min) (mg%)	S.Cr (120Min) (mg%)	Mean S.Cr2 (mg%)	e GFR 2 (mL/min)	Urine PCR (0 min)	Urine PCR (120 min)	Renal Function	GROUP
1	T1	62	M	51	167	Underweight	180	316	8	O.8	O.8	69.06	0.9	0.8	0.85	65	N	A	F	III
2	T2	58	M	58	160	Normal	168	302	8	0.85	0.85	77.71	0.8	0.8	0.8	82.56	N	A	I	II
3	T3	56	F	65	160	Overweight	138	202	6	0.9	0.9	71.62	0.8	0.6	0.75	85.94	N	N	N	I
4	T4	37	M	66	154	Overweight	132	248	3	1.15	1.15	82.1	1	0.8	0.9	104.9	N	N	N	I
5	T5	45	F	55	151	Normal	147	220	5	0.8	0.8	77.1	0.8	0.6	0.7	88.06	N	N	N	I
6	T6	65	M	60	162	Normal	174	298	12	0.9	0.9	69.44	1	1	1	62.5	N	A	F	III
7	T7	56	M	57	176	Underweight	126	184	5	1	1	66.5	0.8	0.8	0.8	83.12	N	N	N	I
8	T8	50	F	47	160	Underweight	112	138	5	0.7	0.7	71.33	0.7	0.6	0.65	76.83	N	N	N	I
9	T9	49	F	49	142	Normal	152	243	8	0.7	0.7	73.54	0.6	0.6	0.6	85.8	N	A	I	II
10	T10	60	M	45	162	Underweight	166	348	9	0.8	0.8	62.5	0.8	0.7	0.75	66.66	N	A	I	II
11	T11	52	M	76	165	Overweight	216	324	7	1.15	1.15	80.77	1.1	1.1	1.1	84.12	N	A	I	II
12	T12	60	F	68	155	Overweight	178	298	7	0.9	0.9	71.35	1	0.6	0.8	80.28	N	A	I	II
13	T13	45	M	70	160	Overweight	146	224	5	1.1	1.1	89.62	1	0.8	0.9	102.62	N	N	N	I
14	T14	67	F	48	162	Underweight	168	287	7	0.65	0.65	63.64	0.6	0.6	0.6	68.94	N	A	I	II
15	T15	59	F	62	166	Normal	198	302	12	0.9	0.9	65.87	1	0.9	0.95	62.4	N	A	F	III
16	T16	60	M	68	156	Overweight	196	344	9	1.05	1.05	71.95	1.1	1.1	1.1	68.42	N	A	F	III
17	T17	55	F	75	157	Overweight	137	206	4	0.9	0.9	83.62	1	0.6	0.8	94.07	N	N	N	I
18	T18	45	M	65	165	Normal	178	320	9	0.9	0.9	95.29	1	0.8	0.9	95.29	N	A	F	III
19	T19	55	M	74	160	Overweight	164	302	5	1.1	1.1	79.11	1	0.9	0.95	91.95	N	A	I	II
20	T20	43	M	63	160	Normal	130	210	5	1	1	84.8	1	0.6	0.8	106.09	N	N	N	I
21	T21	62	F	45	158	Underweight	212	330	11	0.65	0.65	63.75	0.7	0.6	0.65	63.75	N	A	F	III

MASTER CHART (Page 2 out 5)

S.NO	ID	Age in yrs	sex	weight (kg)	height (cms)	BMI (Kg/M²)	FBG (mg%)	PPBG-2hr (mg%)	Duration of DM in yrs	S.Cr (0 min) (mg%)	Mean S.Cr1 (mg%)	e GFR1 (mL/min)	S.Cr (60Min) (mg%)	S.Cr (120Min) (mg%)	Mean S.Cr2 (mg%)	e GFR 2 (mL/min)	Urine PCR (0 min)	Urine PCR (120 min)	Renal Function	GROUP
22	T22	32	F	52	153	Normal	138	256	4	0.9	0.9	73.66	0.8	0.6	0.7	94.69	N	N	N	I
23	T23	57	M	61	164	Normal	186	272	10	1.05	1.05	66.97	1.2	1	1.1	63.68	N	A	F	III
24	T24	42	M	54	170	Underweight	136	280	3	0.8	0.8	91.88	0.8	0.6	0.7	105	N	N	N	I
25	T25	60	F	51	152	Normal	170	268	6	0.8	0.8	60.18	0.8	0.6	0.7	68.81	N	N	N	I
26	T26	55	F	60	164	Normal	146	278	4	0.85	0.85	70.83	0.8	0.7	0.75	80.27	N	N	N	I
27	T27	46	M	68	158	Overweight	128	246	4	1.1	1.1	80.4	1	0.8	0.9	98.64	N	N	N	I
28	T28	46	M	48	163	Underweight	131	215	4	0.8	0.8	78.33	0.6	0.6	0.6	104.44	N	N	N	I
29	T29	55	M	48	146	Normal	138	216	4	0.9	0.9	62.96	1	0.5	0.75	75.55	N	N	N	I
30	T30	44	F	50	165	Underweight	144	232	5	0.85	0.85	66.66	0.8	0.6	0.7	80.95	N	N	N	I
31	T31	57	M	69	159	Overweight	208	278	11	1.05	1.05	75.55	1.2	1.1	1.15	69.16	N	A	F	III
32	T32	65	F	68	148	Overweight	212	234	13	0.95	0.95	63.37	1	1	1	60.2	N	A	F	III
33	T33	51	M	62	165	Normal	128	240	5	1	1	76.64	1	0.6	0.8	95.8	N	N	N	I
34	T34	50	F	67	145	Overweight	135	268	4	0.9	0.9	79.09	0.8	0.6	0.7	101.69	N	N	N	I
35	T35	54	M	56	158	Normal	128	198	5	0.9	0.9	74.32	0.8	0.6	0.7	95.55	N	N	N	I
36	T36	55	F	44	143	Normal	122	196	4	0.8	0.8	63.63	0.8	0.6	0.7	72.72	N	N	N	I
37	T37	55	M	61	162	Normal	194	320	10	1	1	70.01	1.1	1	1.05	68.58	N	A	F	III
38	T38	65	F	68	148	Overweight	212	234	13	0.95	0.95	63.37	1	1	1	60.2	N	A	F	III
39	T39	50	M	53	154	Normal	134	240	6	0.9	0.9	73.61	1	0.6	0.8	82.81	N	N	N	I
40	T40	48	F	55	150	Normal	138	238	3	0.9	0.9	68.53	0.8	0.6	0.7	85.33	N	N	N	I
41	T41	56	M	62	158	Normal	132	244	5	1	1	72.33	0.8	0.9	0.85	85.09	N	N	N	I
42	T42	58	M	61	164	Normal	136	202	6	1	1	69.47	0.8	0.8	0.8	86.84	N	N	N	I

MASTER CHART (Page 3 out 5)

S.NO	ID	Age in yrs	sex	weight (kg)	height (cms)	BMI (Kg/M²)	FBG (mg%)	PPBG-2hr (mg%)	Duration of DM in yrs	S.Cr (0 min) (mg%)	Mean S.Cr1 (mg%)	e GFR1 (mL/min)	S.Cr (60Min) (mg%)	S.Cr (120Min) (mg%)	Mean S.Cr2 (mg%)	e GFR 2 (mL/min)	Urine PCR (0 min)	Urine PCR (120 min)	Renal Function	GROUP
43	T43	55	F	61	164	Normal	146	248	5	1	1	61.21	1	0.8	0.9	68.01	N	N	N	I
44	T44	57	M	55	173	Underweight	122	168	2	0.8	0.8	79.45	0.6	0.6	0.6	105.67	N	N	N	I
45	T45	56	F	57	153	Normal	126	240	6	0.8	0.8	70.65	0.8	0.6	0.7	80.75	N	N	N	I
46	T46	55	M	48	146	Normal	138	216	4	0.9	0.9	62.96	1	0.5	0.75	75.55	N	N	N	I
47	T47	60	M	50	165	Underweight	152	240	6	0.8	0.8	69.44	0.7	0.8	0.75	74.07	N	A	I	II
48	T48	57	M	48	163	Underweight	145	214	5	0.8	0.8	69.16	0.7	0.5	0.6	92.22	N	N	N	I
49	T49	65	F	53	148	Normal	178	280	11	0.75	0.75	62.57	1	0.8	0.9	52.14	N	A	F	III
50	T50	60	F	58	160	Normal	196	328	9	0.9	0.9	60.86	0.9	0.7	0.85	63.82	N	A	I	II
51	T51	53	M	52	168	Underweight	130	242	4	0.95	0.95	66.14	0..9	0.7	0.8	78.54	N	N	N	I
52	T52	44	F	50	165	Underweight	144	232	5	0.85	0.85	66.66	0.8	0.6	0.7	80.95	N	N	N	I
53	C1	47	M	74	162	Overweight	98	136	0	0.9	0.9	106.2	0.9	0.8	0.85	114.86	N	N	N	I
54	C2	38	M	45	156	Underweight	69	118	0	0.75	0.75	85	0.7	0.6	0.65	100	N	N	N	I
55	C3	64	F	56	158	Normal	102	128	0	0.7	0.7	73.67	0.8	0.5	0.65	79.33	N	N	N	I
56	C4	60	F	43	154	Underweight	108	136	0	0.65	0.65	62.48	0.6	0.6	0.6	67.68	N	A	N	I
57	C5	39	M	62	159	Normal	106	128	0	1	1	86.97	1	0.6	0.8	108.71	N	N	N	I
58	C6	50	F	50	150	Normal	98	138	0	0.8	0.8	66.4	0.8	0.6	0.7	75.89	N	N	N	I
59	C7	36	M	48	164	Underweight	102	136	0	0.7	0.7	99.04	0.7	0.5	0.6	117.77	N	N	N	I
60	C8	60	F	56	165	Normal	94	132	0	0.8	0.8	66.04	0.7	0.5	0.6	88.14	N	N	N	I
61	C9	69	F	67	154	Overweight	104	136	0	0.9	0.9	62.39	1	0.6	0.8	72.17	N	N	N	I
62	C10	56	M	72	164	Overweight	98	138	0	1	1	94	1	0.7	0.85	101.17	N	N	N	I
63	C11	50	F	47	160	Underweight	106	138	0	0.7	0.7	74.5	0.6	0.6	0.6	86	N	N	N	I

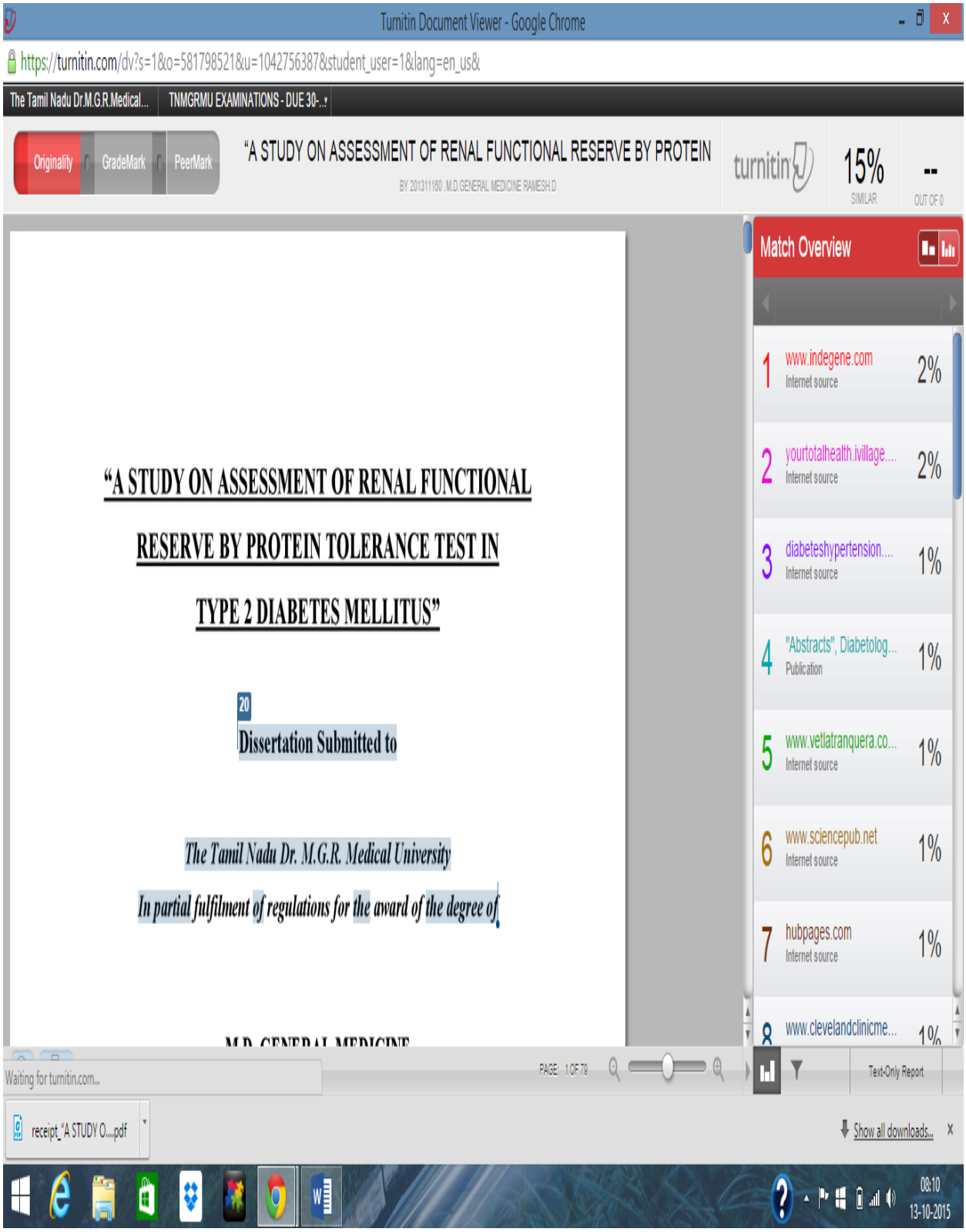
MASTER CHART (Page 4 out 5)

S.NO	ID	Age in yrs	sex	weight (kg)	height (cms)	BMI (Kg/M²)	FBG (mg%)	PPBG-2hr (mg%)	Duration of DM in yrs	S.Cr (0 min) (mg%)	Mean S.Cr1 (mg%)	e GFR1 (mL/min)	S.Cr (60Min) (mg%)	S.Cr (120Min) (mg%)	Mean S.Cr2 (mg%)	e GFR 2 (mL/min)	Urine PCR (0 min)	Urine PCR (120 min)	Renal Function	GROUP
64	C12	45	M	62	158	Normal	96	124	0	1.1	1.1	74.36	0.9	0.8	0.85	98.26	N	N	N	I
65	C13	56	M	58	156	Normal	98	126	0	1	1	67.66	0.6	0.8	0.7	101.26	N	N	N	I
66	C14	40	F	54	152	Normal	66	108	0	0.85	0.85	74.99	0.7	0.6	0.65	98.07	N	N	N	I
67	C15	35	M	45	144	Normal	82	120	0	0.7	0.7	93.75	0.6	0.6	0.6	111.45	N	N	N	I
68	C16	48	F	55	154	Normal	82	130	0	0.9	0.9	66.37	0.8	0.5	0.65	95.89	N	N	N	I
69	C17	49	F	50	142	Overweight	94	132	0	0.75	0.75	71.62	0.6	0.5	0.55	101.95	N	N	N	I
70	C18	37	M	52	170	Underweight	110	137	0	0.85	0.85	87.51	0.6	0.8	0.7	108.33	N	N	N	I
71	C19	59	M	60	158	Normal	94	138	0	1	1	67.5	0.7	0.8	0.75	92.22	N	N	N	I
72	C20	56	F	70	147	Overweight	86	132	0	1	1	69.41	0.8	0.7	0.75	96.96	N	N	N	I
73	C21	54	F	46	162	Underweight	98	132	0	0.7	0.7	66.71	0.6	0.6	0.6	79.65	N	N	N	I
74	C22	50	M	46	158	Underweight	98	125	0	0.8	0.8	71.87	0.8	0.6	0.7	82.14	N	N	N	I
75	C23	59	F	62	160	Normal	72	132	0	0.95	0.95	62.4	0.8	0.7	0.75	81	N	N	N	I
76	C24	57	M	56	158	Normal	96	136	0	0.8	0.8	80.6	0.7	0.7	0.7	94.44	N	N	N	I
77	C25	59	F	44	158	Underweight	76	134	0	0.7	0.7	60.1	0.6	0.6	0.6	90.31	N	N	N	I
78	C26	60	M	78	164	Overweight	102	140	0	1	1	86.66	1	0.7	0.85	104.5	N	N	N	I
79	C27	50	F	50	148	Normal	82	116	0	0.75	0.75	70.83	0.6	0.5	0.55	96.59	N	N	N	I
80	C28	50	F	53	145	Overweight	106	126	0	0.7	0.7	80.44	0.6	0.5	0.55	104.66	N	N	N	I
81	C29	47	M	53	170	Underweight	92	136	0	0.75	0.75	91.27	0.6	0.7	0.65	107.58	N	N	N	I
82	C30	57	F	50	150	Normal	88	126	0	0.7	0.7	69.99	0.6	0.6	0.6	85.51	N	N	N	I
83	C31	60	M	68	164	Overweight	90	134	0	1	1	75.55	0.8	0.6	0.7	107.93	N	N	N	I
84	C32	43	F	66	164	Normal	96	126	0	0.85	0.85	88.91	0.8	0.6	0.7	110.19	N	N	N	I

MASTER CHART (Page 5 out 5)

S.NO	ID	Age in yrs	sex	weight (kg)	height (cms)	BMI (Kg/M²)	FBG (mg%)	PPBG-2hr (mg%)	Duration of DM in yrs	S.Cr (0 min) (mg%)	Mean S.Cr1 (mg%)	e GFR1 (mL/min)	S.Cr (60Min) (mg%)	S.Cr (120Min) (mg%)	Mean S.Cr2 (mg%)	e GFR 2 (mL/min)	Urine PCR (0 min)	Urine PCR (120 min)	Renal Function	GROUP
85	C33	50	M	70	168	Overweight	108	132	0	1.2	1.2	72.91	1.2	0.7	0.95	92.1	N	N	N	I
86	C34	60	F	50	152	Normal	92	136	0	0.75	0.75	62.96	0.7	0.5	0.6	78.7	N	A	I	II
87	C35	36	M	70	168	Normal	86	126	0	1.05	1.05	96.29	0.9	0.8	0.85	118.95	N	N	N	I
88	C36	55	M	60	158	Normal	94	132	0	1	1	70.83	0.7	0.8	0.75	98.88	N	N	N	I
89	C37	60	F	60	152	Overweight	98	108	0	0.9	0.9	62.96	0.8	0.7	0.75	75.55	N	N	N	I
90	C38	48	F	74	165	Overweight	104	138	0	1	1	80.37	1	0.6	0.8	102.64	N	N	N	I
91	C39	58	M	54	152	Normal	68	116	0	0.75	0.75	82	0.6	0.6	0.6	105	N	N	N	I
92	C40	58	F	52	168	Underweight	98	126	0	0.8	0.8	62.92	0.8	0.5	0.65	77.44	N	N	N	I
93	C41	40	M	64	162	Normal	84	128	0	0.95	0.95	93.56	0.8	0.8	0.8	111.11	N	N	N	I
94	C42	56	F	78	164	Overweight	64	110	0	0.95	0.95	81.42	0.9	0.8	0.8	101.29	N	N	N	I
95	C43	59	M	58	155	Normal	64	116	0	0.85	0.85	76.76	0.9	0.6	0.75	89.14	N	N	N	I
96	C44	60	M	60	158	Normal	104	140	0	1	1	66.66	0.9	0.9	0.9	70.17	N	A	I	II
97	C45	49	M	54	153	Normal	74	128	0	0.8	0.8	85.31	0.7	0.6	0.65	109.61	N	N	N	I
98	C46	67	F	51	148	Normal	76	124	0	0.7	0.7	62.78	0.6	0.5	0.55	82.1	N	N	N	I
99	C47	66	M	60	158	Normal	85	124	0	0.9	0.9	68.51	0.7	0.6	0.65	108.33	N	N	N	I
100	C48	36	M	56	174	Underweight	76	139	0	0.9	0.9	89.87	0.8	0.8	0.8	105	N	N	N	I
101	C49	42	F	60	158	Normal	74	128	0	0.85	0.85	81.7	0.8	0.8	0.8	86.8	N	N	N	I
102	C50	47	F	48	161	Underweight	62	118	0	0.7	0.7	75.28	0.6	0.6	0.6	91.61	N	N	N	I
103	C51	60	M	54	172	Underweight	90	134	0	0.9	0.9	66.66	0.9	0.6	0.75	82	N	N	N	I
104	C52	43	M	67	169	Normal	92	136	0	0.9	0.9	100.3	0.8	0.8	0.8	112.8	N	N	N	I

PLAGIARISM CERTIFICATE



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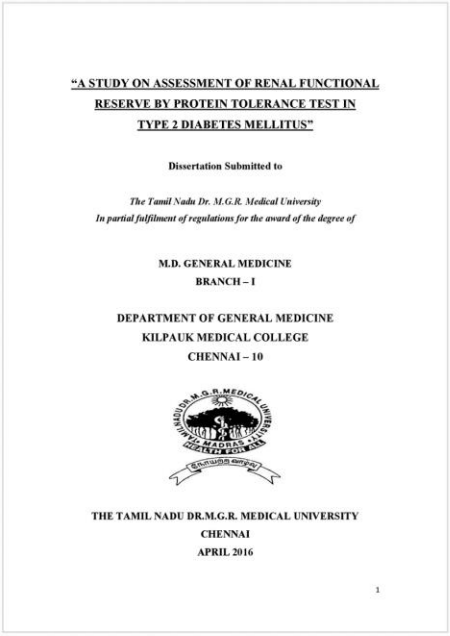


"A STUDY ON ASSESSMENT OF RENAL FUNCTIONAL RESERVE BY PROTEIN TOLERANCE TEST IN TYPE 2 DIABETES MELLITUS"

Dissertation Submitted to

The Tamil Nadu Dr. M.G.R. Medical University
In partial fulfilment of regulations for the award of the degree of

M.D. GENERAL MEDICINE
BRANCH – I

DEPARTMENT OF GENERAL MEDICINE
KILPAUK MEDICAL COLLEGE
CHENNAI – 10

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI
APRIL 2016

1

PROFORMA

PERSONAL DETAILS:

NAME: ID: ADDRESS:

AGE:

SEX:

Height: Weight: BMI:

Medical History:

Diabetes: Yes/No Duration of DM:

Hypertension: yes / no Renal Disease: yes /no

Diabetic Nephropathy: yes / no

Diet History: veg /Non veg: Drug History:

Personal History: Family History:

Physical examination:

Pulse: BP: Temp: RR:

CVS: RS: ABDOMEN: CNS:

Investigations: Blood Sugar: FBG: 2hour PPBG:

Protein Tolerance Test:

Serum Creatinine:

Fasting: e GFR1:

After Protein Meal @60min: 120min: mean: e GFR2:

Urine PCR: 0min: 120min:

Renal Function Result: (Tick)

No Evidence of Renal Dysfunction - Normal (N) ☐

Evidence of Renal injury - Injury (I) ☐

Evidence of incipient Renal Failure - Failure (F) ☐

INFORMED CONSENT FORM

நோயாளி ஒப்புதல் படிவம்

ஆராய்ச்சியின் விவரம்:

ஆராய்ச்சி மையம்: அரசு ராயப்பேட்டை மருத்துவமனை

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்துகொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்திக் கொண்டேன்.
2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்புமின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முழுமையான உரிமை உள்ளதையும், இதற்கு எவ்வித சட்ட பிணைப்பும் இல்லை என்பதையும் அறிவேன்.
3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஒழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிகளுக்காகவோ பயன்படுத்திக்கொள்ளலாம் என்றும் மேலும் இந்த நிபந்தனை நான் இவ்வராய்ச்சியிலிருந்து விலகினாலும் தகும் என்றும் ஒப்புக்கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் (சட்டபூர்வமான தேவைகள் தவிர) வெளியிடப்படமாட்டது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்பு தெறிவிக்கமாட்டேன் என்று உறுதியளிக்கின்றேன்.

4. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கின்றேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன் என்றும் உறுதியளிக்கின்றேன்.
5. இந்த ஆராய்ச்சிக்குத் தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்பு தருவேன் என்று உறுதியளிக்கின்றேன்.
6. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புறுத்தலுமின்றி எனது சொந்த விருப்பத்தின் பேரிலும் சுயஅறிவுடனும் முழுமனதுடனும் சம்மத்திக்கின்றேன் என்று இதன் மூலம் ஒப்புக்கொள்கிறேன்.

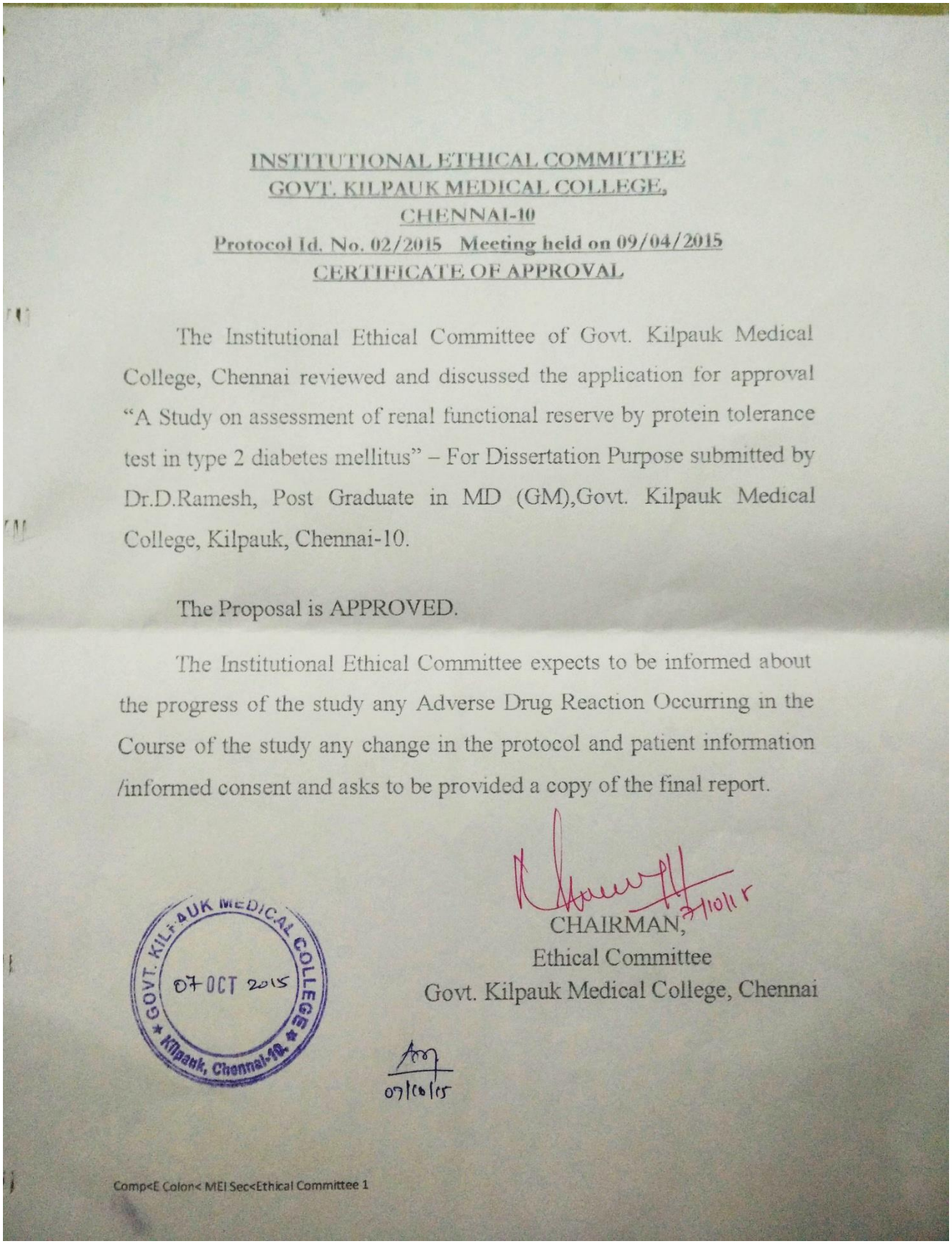
நோயாளியின் கையொப்பம் / பெருவிரல் கைரேகை

இடம்: தேதி:

ஆராய்ச்சியாளரின் கையொப்பம்

இடம்: தேதி:

ETHICAL COMMITTEE APPROVAL CERTIFICATE



INSTITUTIONAL ETHICAL COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol Id. No. 02/2015 Meeting held on 09/04/2015
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on assessment of renal functional reserve by protein tolerance test in type 2 diabetes mellitus" – For Dissertation Purpose submitted by Dr.D.Ramesh, Post Graduate in MD (GM),Govt. Kilpauk Medical College, Kilpauk, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

CHAIRMAN,
Ethical Committee
Govt. Kilpauk Medical College, Chennai

GOVT. KILPAUK MEDICAL COLLEGE
07 OCT 2015
Kilpauk, Chennai-10.

07/10/15

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